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Field Training of Army Medical Officers

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EXAMINATION of our history and that of other great nations will reveal that major wars have occurred about every 20 to 25 years. These wars last from 2 to 4 years. If this state of affairs continues most doctors will probably experience two wars in their professional lifetime. Thus one-fifth to one-sixth of a doctor's professional life will be in a wartime practice.

An essential mission of the Medical Department is the preparation for the support of the combatant arms under wartime conditions. In the transition period following World War II the training desirable for this preparation has not been stressed. We have relied on the fact that most of our Regular Army officers had received ample training during the last war period. The changing concept of future warfare, organizational changes, and the constant development of new weapons of offense and defense make it advisable to bring these more experienced officers up to date. In the Regular Army Medical Corps we have an ever-increasing number of physicians who do not have war experience.

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The unique features of medical practice required for the maintenance of health, prevention of disease and injury, and the care and rehabilitation of casualties under wartime conditions should be an important part of every medical officer's training. Orientation courses and other training in these subjects should be given early in a medical officer's career. This training is in addition to the usual residency and practical studies leading to proficiency in curative methods and toward certification by an American specialty board although it is believed that when it is properly developed the two will be closely intermingled. This type of training should increase a doctor's competence and appreciation of the professional requirements needed in a medical service during war.

There should be an early close correlation of professional medicine and the elements of administrative, staff, and command duties. By intelligent exposure doctors will undoubtedly emerge with special interest and talent in administrative, staff, and command work. They should be encouraged. These officers should be allowed to specialize, receiving opportunity for recognition and advancement equal to those of officers in any other chosen career field. With this concept in mind we should expect our specialized medical field personnel to be better trained and more actively interested in the aspects of military medicine. Conversely, our specialists in curative and preventive medicine would know the specific phases required in war and be reasonably well versed in medical field duties dealing with administration, staff, and command.

Using the previously described methods, we hope to develop capable medical officers for field duty with a constructive interest in their field of endeavor. This should give adequate medical support to field commanders and provide trained personnel for medical services in the field.

In order to aid us in meeting this need, authorization has been secured to start the Medical Department Company Officers' Course this fall. Phase I of this course will be given at the Medical Field Service School, Brooke Army Medical Center, Fort Sam Houston, Tex., and Phase II at the Army Medical Department Research and Graduate School, Washington, D. C. Phase I will open 5 September 1950 and close 2 February 1951. Phase II will open 12 February 1951 and close 29 June 1951. In addition to medical officers, dental, veterinary, and Medical Service Corps officers will attend Phase I. Only medical officers will attend Phase II.

It is planned that each officer entering the Medical Corps will have the opportunity of taking this course. Phase I will provide basic branch training to officers so that they will be thoroughly grounded

in the duties and responsibilities appropriate to company grade Medical Department officers. Phase II will provide instruction in the unique aspects of military medical practice required to supplement basic medical knowledge in the prevention, treatment, and rehabilitation of casualties as they occur in war.

This course should come as early in an officer's career as possible, preferably immediately after he has been commissioned in the Regular Army. The course should be followed by a period in which he can apply his instruction. During this period, which will usually not exceed 2 years, his duties may include assignment to a tactical medical unit. While undergoing this training in Army field medicine, he will learn the matériel and personnel means with which he will have to work in fulfilling his mission as an army field surgeon in the medical command and staff career. He will become acquainted with the rudiments of the tactics of the unit with which he serves. Most important, he will be learning to practice his profession under field conditions.

Later, between his fifth and twelfth years of service, each officer will have the opportunity to attend the advanced course at the Medical Field Service School, Brooke Army Medical Center. This course is designed to provide instruction in the light of war lessons and modern developments to insure effective development of all Medical Department units within the framework of the Department of the Army. Efficient medical support of military forces includes orientation in the organization and employment of divisions, corps, field armies and the related medical, dental, and veterinary services. Instruction is presented primarily from a staff and command viewpoint. This may be followed by a tour of duty as a division or corps surgeon, or duty in the office of an army or theater surgeon, or in the medical section of the Office, Chief of Army Field Forces.

The atomic era is here with its possibilities for producing enormous numbers of military and civilian casualties. This demands that every Regular Army Medical Department officer be fully trained in the peace years in the procedures applicable to the medical control and supervision of large scale disasters.

It is anticipated that enough officers to fulfill all requirements will become interested to the point of electing Army Field Medicine as a career. In peacetime only a few specialists in this field are required. They will consist of carefully selected officers who wish to follow this course and who show special aptitude for it. The career contemplated for medical command and staff officers will consist of attendance at certain service schools whose courses are of particular interest to the Medical Department. Specifically these are: (*a*) The Medical Field Service School; (*b*) The Infantry School at Fort Benning, Ga., The Artillery School at Fort Sill, Okla., or the Armored School at

Fort Knox, Ky.; (*c*) a post-graduate course in preventive medicine at the Army Medical Department Research and Graduate School; (*d*) The Command and General Staff College at Fort Leavenworth, Kans., (*e*) The Armed Forces Staff College at Norfolk, Va.; (*f*) The Army War College, The Industrial College of the Armed Forces; and (*g*) The National War College.

These school periods will be alternated with applicatory tours of duty with field medical units and refresher professional assignments in Army hospitals. This last item is considered of particular importance, for it is essential that medical command and staff officers keep fully abreast of every element of medical progress. Final goals for these officers will be such assignments as army or theater surgeons, instructors at one of the special or general service schools, duty in the medical section of the Office, Chief of Army Field Forces, or in one of the divisions of the Surgeon General's Office, or similar staff positions.

This is a brief outline of the instruction and training that is planned in order to prepare medical officers for their duties in Army Field Medicine. It also outlines in general the career that will be offered to those few carefully selected officers who show special aptitude and a desire to specialize in Army Field Medicine.

Fundamentals in the Use and Preservation of Homogenous Bone

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THE present-day use of preserved grafts of homogenous bone was fostered by Bush and Garber (*3*) in 1945. The large number of bone banks in existence today attests to their clinical value. There is little doubt that the principles of bone preservation and the surgical application of preserved bone is a permanent although, as yet, undetermined advance in orthopedics.

The physician in charge of a bone bank who does not appreciate the fundamentals of supervision will find that not only will such a bone bank fail to be of value, but also that the clinical failures that will occur may greatly delay acceptance of a fundamentally satisfactory procedure in orthopedic surgery.

One major disadvantage of the present-day methods is the lack of unequivocal control of the asepsis of the deposit. The culture of a single specimen is inadequate and proper bacteriologic determination requires culture of the entire bone graft. Therefore, some institutions rely solely upon donor wound healing as the criterion for an acceptable bone deposit. Both of these methods have disadvantages but they have proved to be clinically worthwhile in the hands of many surgeons.

The development of a simple method of sterilizing bone grafts which would not materially damage the osteogenetic properties of the deposit or so alter it as to make it unsatisfactory in osteosynthesis would be a signal advance.

It is estimated that although frozen homogenous bone is approximately 15 to 50 percent slower in final healing than its autogenous counterpart, the end results are identical (*1*). Key (*2*) observed that procurement of an autogenous bone graft increases the gravity

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of the operative procedure about one-third. The experimental and clinical work relating to homogenous bone grafts by Bush and Garber (*3*), Wilson (*4*), Walsh (*5*), Lipscomb (*6*), Weaver (*7*), Reynolds and Oliver (*8*), Inclan (*9*), and Zimbron (*10*) indicated that the present methods of chemical and refrigerative preservation are most satisfactory. However, these present-day methods of bone preservation are only milestones in the quest for a bone graft substitute that will be perfectly and quickly revascularized, completely acceptable to the host, and readily available.

HISTORY

In 1867 Ollier (*11*) published his treatise on bone formation. His experimental and clinical observations are the basis of autogenous bone grafting as we know it today. We find the first reference to the value of refrigeration in the preservation of bone when he determined that temperatures of less than −16° C. (3.2° F.) delayed putrefaction of bone. He also found that rabbit bone kept at −1° C. (30.2° F.) gave a growth of bone four times greater than that of rabbit bone kept at 5° to 10° C. (41.0° to 50.0° F.). He also commented on the practicality of using cadaver bone in human bone grafting.

Tuffier (*12*), in 1910 and 1911, preserved, in an ordinary ice box, pieces of human fat, bone, cartilage, and peritoneum which had been placed in petrolatum. Although there are several references in this older literature to the clinical use of this refrigerated human cartilage and peritoneum, it was noted that portions of dog periosteum, which had been kept in cold storage for from 24 to 48 hours, when transplanted under the skin of the chest of another dog would produce bone. In this same period Albee (*14*) published one of the first standards for the preservation of homogenous grafts; the graft was to be either immersed in petrolatum or wrapped in sterile petrolatum gauze and placed in storage at a temperature of 4° to 5° C. (39.2° to 41.0° F.). He considered freezing undesirable as "the resultant contraction and expansion damage the cellular content of the graft" (*15*). Fresh and cadaver bone were successfully used after chilling for from 24 to 48 hours. That these principles have gained partial acceptance in orthopedic centers can be verified by their inclusion in the Medical Manual No. 4, Military Orthopedic Surgery (World War I).

In 1918, Groves (*16*) reported that there had been sufficient success in the use of chilled homogenous grafts to justify their employment in selected cases if the correction of a defect included all or part of the cartilagenous articular surface of the long bones. He noted that such a graft should have the articular configuration necessary for proper modeling and recommended that the graft be obtained

from a cadaver free from infectious disease; preferably one whose death was caused by trauma. After the graft was taken, it was to be cultured and placed in a sterile receptacle in an ice chest and after 24 hours, if the culture was negative, the graft could be used. These concepts are remarkably parallel to the present use of frozen cadaver bone.

The recommended practices of Albee and Groves did not seem to gain general acceptance, possibly because of the difficulties of procurement and of preservation. No further reports on the clinical use of bone preserved by chilling or freezing appeared in the literature until late in World War II.

In 1934, Keith (*17*) noted "survival" of some cells with new bone formation, following immersion of fragments of dog bone for 10 minutes in liquid air. A similar result was obtained with implantation of dog carpal and tarsal bones frozen for 10 minutes in liquid air.

Between 1931 and 1937, Orell (*18*) published his work on preserved heterogenous bone. He defined os purum as bone which, through a lengthy physiochemical process, was freed of fat, connective tissue, and protein; however, it was not entirely freed of all collagenous matrix. Os novum was then produced by subperiosteal implanting with subsequent grafting after 1 to 2 months.

In 1937, Smith (*19*) reported two successful homogenous grafts in nonunion of fractures in osteogenesis imperfecta. The bone was refrigerated for preservation and autoclaved immediately before use.

Inclan (*9*) in 1942, was the first to utilize refrigeration in the preservation of homogenous bone for an appreciable number of bone grafts. He utilized these preserved homogenous grafts in 8 cases, 6 of which were successful; preserved autogenous bone was used for the remaining 46 grafts. The transplant was placed in a sterilized glass container and covered with the patient's own blood or that of a donor of the same group. The maximum preservation time was 63 days. The minimum was 3 days and good or excellent results were obtained in approximately 75 percent of the cases.

In 1942, Smith (*20*) employed homogenous bone refrigerated 18 days with apparently satisfactory results.

The advent of better refrigeration methods and the mass production of antibiotics proved to be a great stimulus to bone graft surgery and resulted in the increased use of frozen bone transplants.

A type of frozen-bone bank was initiated by Bush and Garber (*3*) (*21*) in 1945. It was prompted by a need for additional bone for orthopedic procedures involving extensive spinal fusions for severe scoliosis, low back disorders, filling of bone cysts, and the replacement

of other benign defects in bone. At first, bone was preserved at temperatures ranging from −2° to −5° C. (28.4° to 23.0° F.); however, it was observed that bone could be preserved for only 2 or 3 weeks. Following experimental studies in animals it was found that −24° C. (−11.2° F.) was probably the optimum temperature for prolonged preservation of bone for grafting purposes. In 126 procedures in which the frozen homogenous graft was used, they noted 2 infections, 1 fracture of an onlay graft, and 1 failure because of inadequate soft tissue coverage. In an effort to maintain strict asepsis, the fresh graft (without preservative) was placed in a double jar (a small jar within a large one) and covered with a sterile rubber dam.

Subsequently, Wilson (*4*) reported 30 surgical procedures in which fresh bone without preservative added was placed in a single sterile sealed jar and frozen at −22° to −30° C. (−7.6° to −22.0° F.). No infections were reported and in all cases "its behavior seemed to be identical to that of the fresh autogenous bone." At a later date, Wilson reported over 200 cases of the clinical use of frozen bone with satisfactory results; the infection rate was approximately 2 percent.

Walsh (*5*), working independently, presented a similar method of preserving bone by refrigeration. This work is the best review of the fundamentals of the use of freezing temperatures in the prolonged preservation of bone.

The impetus given to the use of frozen bone by the previous workers cannot be underestimated. In 5 years, the bone bank has grown from an experiment to an established orthopedic practice, even though the indications for the use of frozen bone are subject to limitations.

THE ACTION OF REFRIGERATION IN THE PRESERVATION OF BONE

According to Walsh (*5*) the changes which occur in stored bone may be classified into two groups: (*a*) biochemical changes in the activity of the enzymes of the bone itself; and (*b*) changes due to the action of putrefactive bacteria. To this may be added (*c*) changes in the bone due to mechanical action of freezing.

Lipscomb (*6*) has demonstrated that alkaline phosphatase activity is demonstrable after 2 to 3 weeks of bone storage at temperatures of −10° C. (14.0° F.). Gross, histologic, and chemical examinations following experimental procedures in rabbits indicate that the activity of this enzyme has no notable effect upon the final healing of the frozen bone graft. Frozen specimens examined grossly, microscopically, and by olfaction revealed no evidence of putrefaction. Weaver (*7*) who has used frozen homogenous bone successfully after 308 days' storage in an ordinary ice-cream cabinet noted no gross changes. Walsh found that bone removed aseptically from an ampu-

tated limb and stored for 10 months at −22° C. (−7.6° F.) revealed no gross changes.

It is possible that partial protein denaturation occurs in the bone as a direct result of freezing. Hardy (*22*) observed that gels, which were singularly refractive to polarized light previous to freezing, became doubly refractive during the frozen state. It is known that "freezing and thawing alter the configuration of colloidal systems whether gels of sols and the resulting structures depend upon the rate of freezing" (*23*). This is evidence that the colloidal molecular structure impairment is permanent. In a bone transplant, autogenous or homogenous, it is possible that the organic fraction of the calcium proteinate may be an important factor in facilitating the subsequent revascularization of the graft. Perhaps freezing alters the osseous protein and if we consider that the majority of all transplant grafts die, this may explain the estimated 15 to 50 percent delay in healing after the use of frozen bone grafts. Moran (*23*) has noted that the temperature at which the mixture of colloid and ice forms must be lower than the external temperature due probably to the low diffusibility of the colloid complexes. Hardy (*22*) found that gels at 65.6 percent concentration could not be made to freeze.

These observations have been applied to frozen bone on the basis that bound water is intracellular and cannot be frozen; and interstitial water is not so bound to protein and hence can be frozen (*22*). Further the internal friction increases as the colloid concentration increases and as the temperature falls. This is the result of the inability of ice-forming sources to overcome internal friction (*22*) and this prohibits intracellular freezing. Stiles (*24*) believes that the cellular death of the tissue kept at freezing temperature occurs because of formation of ice crystals which alter the space relation of the phases constituting the normal colloid complex of protoplasm.

On the basis of the foregoing, we may conclude that, at the usual bone bank temperatures, freezing of bound water does not occur nor is there serious protein denaturation, and since the potential value of any graft conceivably exists in the protein fraction of the calcium proteinate, the physiologically important protein fractions of the donor bone are preserved. This explanation may be the reason that bone grafts can be preserved by freezing (fig. 1) and in addition offers an explanation for the delay in final bone healing when using frozen bone.

Strumia, McGraw, and Reichel (*25*) have given additional proof of the relationship of cold to colloid preservation by demonstration that, under refrigeration, it is possible to retain the physiochemical properties of complex colloids. The essential conditions are rapid

Figure 1.—A typical bone bank.

freezing, maintenance of a temperature below −15° C. (5.0° F.), and rapid thawing followed by a quick warming to 98° F. They also stated that plasma stored at 4° C. (39.2° F.) gradually lost the entire protein fraction; however at −15° C. (5.0° F.) this did not occur. Finn (*27*) has shown that the protein of juice of muscle stored at −1° to −3° C. (30.2° to 26.6° F.), underwent denaturation of protein up to 10 percent of the volume. If muscle juice was stored at −20° C. (4.0° F.), only 1 percent was denatured; this occurred early and remained constant up to 75 days. Of course, bone protein is not exactly the same as that of blood and muscle juice, however, fundamentally similar proteins tend to follow the same chemical laws.

It appears, therefore, that the optimum temperature for prolonged bone preservation is in a range with a minimum of −15° C. (5.0° F.) and the maximum so much colder that it is yet to be determined.

EFFECT OF REFRIGERATION ON BACTERIA

Haines (*26*) has demonstrated that the critical zone for bacterial survival lies in the temperature range of −1° to −2° C. (30.2° to 28.4° F.). The date of death at −1° C. (30.2° F.), was definitely more rapid than at −5° C. (23.0° F.); there was little variance in the death of the bacteria evaluated. No evidence has been presented that

a bactericidal effect is associated with the rapidity of the freezing process. The sensitivity of bacteria to cold varies greatly; for example, a suspension of *Bacillus pyocyaneus* frozen rapidly to −70° C. (−94.0° F.), when thawed showed that approximately 80 percent of the organisms had been killed. Similar treatment of *Bacillus mesentericus* (a spore-former) killed none.

Turner (*28*) has demonstrated that spirochetes are only slightly adversely affected by temperatures as low as −78° C.; however, at higher temperatures, −10° to −20° C. (14.0° to 4.0° F.), loss of the spirochetes occurred during storage periods.

As a rule, viruses placed in glycerin and maintained at freezing temperatures will remain virulent for a number of weeks; however, there seems to be a considerable fall in titer from that of the fresh specimens. Viruses, such as human influenza, yellow fever, and certain types of encephalomyelitis when frozen and maintained at −78° C., have substantially the same titer after 6 months.

The personal experiences of the author and Dr. A. D. Kenton[2] showed that stock cultures of hemolytic *Staphylococcus aureus* and hemolytic streptococci when placed in the bone bank and kept at −20° to −30° C., revealed a heavy growth of organisms when cultured at weekly intervals for 4 weeks and monthly intervals for 6 months.

From this evidence, it is apparent that the temperature required for adequate bone preservation is bacteriostatic and probably mildly bactericidal.

THE EFFECT OF REFRIGERATION ON MALIGNANCY

The transmission of malignancy by inoculation from one human to another has not, to the author's knowledge, been conclusively proved. The effect of cold upon the transmissibility of human malignancies could not, therefore, be evaluated in the light of clinical experience.

For this reason we have turned to the noteworthy results of the experimental surgeons. Breedis, Barnes, and Furth (*29*) have demonstrated the viability of mouse sarcoma frozen at −30° to 70° C., for 56 days. Their findings indicated that the transmission of leukemia and tumors in frozen tissue is due to the survival of neoplastic cells. Mider and Morton (*30*) using strains of sarcoma and carcinoma found that after freezing rapidly at −74° C., carcinoma transplants gave 45 to 50 percent successful results and the sarcoma gave 85 to 90 percent successful results. Klinke (*31*) observed that transplantable sarcoma and carcinoma would grow after freezing to −250° C. Greene (*32*) believes that the transfer of bone or any other tissue from a cancer

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patient to a normal person carries with it the danger of transferring malignant cells (even if the selected bone is apparently well away from the primary malignancy) and that some malignant osteogenic tumors kept at −25° C., will survive and grow when transplanted to animals. Since many patients who have a malignancy may have segments of normal-appearing bone removed during the course of definitive or palliative surgical procedures, the previous admonition is timely. Coley and Higinbotham (*33*) have used normal-appearing ribs removed during thoracotomies for mediastinal tumors (the majority of which were malignancies) in 16 cases with no unsatisfactory results in short-term follow-ups.

THE MERTHIOLATE BONE BANK

This method for the chemical preservation of homogenous bone was developed by Reynolds and Oliver (*34*). It is similar to the method used for the successful preservation of cartilage. The bone is removed aseptically at operation or autopsy; all soft tissue is removed, the marrow cultured, and the bone transplant is then placed in an aqueous solution of 1:1000 merthiolate for 2 weeks. The bone is then removed from the antiseptic solution, recleaned and recultured under aseptic conditions. This step is necessary, for the mode of action of the antiseptic is protein coagulation and considerable glutinous debris accumulates. The bone is then placed in a 1:5000 solution of merthiolate which is changed monthly or biweekly for the purposes of cleanliness. After two negative cultures, the graft may be used. Reynolds and Oliver (*8*) found that grafts preserved in merthiolate solutions were morphologically similar to autogenous grafts preserved under similar conditions and in some respects were better than frozen grafts. In 71 cases in which the merthiolate grafts were used, 42 were reported successful. The advantages of this method lie in its ready availability, its inexpensive material, and its simple space requirements. It is also being used in those cases in which infection may recur (*35*).

The writer believes the following considerations are to be noted: (*a*) Transferring the bone from a 1:1000 solution to a 1:5000 solution of merthiolate can be compared to transfer from a distinctly bactericidal solution to a much less bactericidal solution. (*b*) The bone is subsequently removed from the 1:5000 solution biweekly for cleaning purposes and thus exposed to the open environment and, just as in other operative procedures, contamination is possible. (*c*) Cultures of bone fragments are not considered to be adequate evaluations of the possible contamination of the deeper portions of any bone. The antiseptic action of the mercurial is dependent upon its ability to coagulate protein. This results in a surface film of protein coagulum

which permits minimal surface penetrations and is easily washed off. The antiseptic value of this bone is questionable when it is placed in the host for the protective and antiseptic-impregnated surface film is usually washed off as a preliminary to surgical installation.

The value of such mercurials apparently is in their preservative actions and their slight to moderate bactericidal value for the protein coagulum is not only bactericidal but may act as a seal preventing excessive tissue dehydration.

THE SURGICAL USE OF PRESERVED BONE GRAFTS

Frozen bone is most commonly applied in the form of chips, slivers, and crumbs. These are of value in such procedures as fusions for scoliosis, severe instability of the lumbosacral articulations, and spondylolistheses. In addition, the implantation of cancellous and cortico-medullary crumbs as an adjunct to fracture treatment by internal metal fixation is a growing practice. This is in keeping with published reports of satisfactory chip-graft results in the experimental animal as well as in man. To date, no experimental evaluation of large preserved homogenous grafts has been reported. Accordingly the use of this type of cortical grafts has not enjoyed the popularity of the smaller cancellous graft. Weaver (*7*) has used corticomedullary preserved bone grafts with equivocal results in some cases. One fundamental to be learned from the preceding is that frozen grafts should not be expected to perform well physiologically when fresh grafts have previously failed under similar circumstances.

DISCUSSION

The disadvantages of preserved homogenous bone grafts are: (*a*) Preserved grafts are not satisfactorily revascularized nor as much of a host stimulus as are the autogenous counterparts. (*b*) Some orthopedic surgeons fear that these preserved graft substitutes will not be adequately revascularized and that, if revascularized, the grafts may not be as acceptable to the host and will "melt away" as does human homogenous skin grafts. (*c*) Other groups believe that not only is it undesirable to take bone from the same patient but also that the free and easy access of bone replacement may prompt unnecessary surgery. (*d*) Some surgeons consider that the present clinical indications are not inclusive enough to warrant the expense of bone-bank equipment and the assignment of personnel. (*e*) The shortage of qualified personnel to assume the responsibilities and duties of administration of a bone bank and, in addition, the necessity of training technicians is, at present, a very practical disadvantage. (*f*) The lack of standardization of indications, methods, and forms

for bone-bank deposits and withdrawals, necessitates considerable loss of time of qualified personnel.

Basically, it is proved that the smaller sections of preserved bone are not only physiologically acceptable but also they are completely albeit slowly revascularized. Since the concept of the bone bank over 5 years ago, there have been no reports indicating graft disappearance or "melting" other than that expected with comparable fresh autogenous graft. The infection rate has not exceeded that expected from any other orthopedic procedure. Wilson (*4*) reported infections in 2 percent in over 200 consecutive cases in which frozen bone was employed. In our experience, the use of a frozen-bone graft with minimal soft-tissue dissection at the operative site is of noteworthy value. Not only has the average operating time been shortened by at least 30 percent but there is less postoperative pain, and the need for sedatives is proportionately diminished. The convalescence is shortened since there is only one operative site to consider. The chronic pain which often characterizes donor sites is now no problem. Supportive measures, such as blood transfusions, that were previously routine in major bone-grafting procedures, are now the exception rather than the rule.

CONCLUSIONS

Frozen bone appears to serve the functions demanded of an osteoplastic transplant and has additional values also, for it acts not only as a "filler" for an osseous defect but it also stimulates active bone formation on the part of the host. It may serve the demands of osteosynthesis and, in addition, stimulate osteogenesis. While frozen homogenous bone is not revascularized as well as its fresh autogenous counterpart and, in the frozen cortical homogenous grafts, the delay may be considerable (*7*), it will ultimately be identical with the host. These factors limit the clinical indication for preserved bone.

The smaller orthopedic institutions would benefit by watchful waiting until development of the present trends in the use of frozen-bone grafts which is having a major trial in the larger institutions. As results are published, the acceptance or rejection of the use of preserved homogenous bone could then be made to fit the needs.

The future of the use of preserved bone, if scientifically controlled, vigorously pursued, and applied with considered and mature surgical judgment, may prove to be of value to every orthopedic surgeon.

REFERENCES

1. LIPSCOMB, P. R., and BONFIDGLIO, R. A.: Personal communication.
2. KEY, J. A.: Choice of operation for delayed nonunion of long bones. Ann. Surg. 118: 665–680, Oct. 1943.

3. BUSH, L. F., and GARBER, C. Z.: The bone bank. J. A. M. A. **137:** 588–594, June 12, 1948.
4. WILSON, P. D.: Experiences with bone bank. Ann. Surg. **126:** 932–946, Dec. 1947.
5. WALSH, A. C.: Thesis: I. Use of homogenous and heterogenous bone in bone grafting. II. Method of preserving homogenous bone for use in bone grafting. Mayo Foundation, 1947.
6. LIPSCOMB, P. R.: Exhibit: Alkaline phosphatase in transplantation of frozen bone. (American Academy of Orthopedic Surgery, 1948.) Mayo Clinic permanent exhibit.
7. WEAVER, J. B.: Experiences in use of homogenous (bone bank) bone. J. Bone & Joint Surg. **31A:** 778–792, Oct. 1949.
8. REYNOLDS, F. C., and OLIVER, D. R.: Clinical evaluation of merthiolate bone bank; a preliminary report. J. Bone & Joint Surg. **31A:** 792–799, Oct. 1949.
9. INCLAN, A.: Use of preserved bone graft in orthopaedic surgery. J. Bone & Joint Surg. **24:** 81–96, Jan. 1942.
10. ZIMBRON, A. V.: Bone Bank (motion picture). Audio-Visual Section, American Academy of Orthopedic Surgery, 1949.
11. OLLIER, L.: Traite Experimental et Clinicque de la Regeneration des os et de la Production Artificialle du tissue osseux. Vols. 1 and 2. Victor Masson et Fils, Paris, 1861. pp. 412–457.
12. TUFFIER: Cited by CARREL, A. (*13*).
13. CARREL, A.: Preservation of tissues and its applications in surgery. J. A. M. A. **59:** 523–527, 1912.
14. ALBEE, F. H.: Bone transplantation as a treatment of Pott's disease, clubfoot, and ununited fractures. Papers on orthopedic surgery in the New York Postgraduate Medical School and Hospital, 1912. pp. 463–485.
15. ALBEE, F. H.: Bone-Graft Surgery. W. B. Saunders Co., Philadelphia, Pa., 1916.
16. GROVES, E. W. H.: Methods and results of transplantation of bone in the repair of defects caused by injury or disease. Brit. J. Surg. **5:** 185–242, Oct. 1917.
17. KEITH, W. S.: Small bone grafts. J. Bone & Joint Surg. **16:** 314–330, Apr. 1934.
18. ORELL, S.: Surgical bone grafting with "os purum," "os novum," and "boiled bone." J. Bone & Joint Surg. **19:** 873–885, Oct. 1937.
19. SMITH, A. DEF.: Use of homologous bone grafts in cases of osteogenesis imperfecta. Arch. Surg. **34:** 687–694, Apr. 1937.
20. SMITH, A. DEF.: Cited by BUSH, L. F., and GARBER, C. Z. (*3*).
21. BUSH, L. F.: Use of homogenous bone grafts; preliminary report on bone bank. J. Bone & Joint Surg. **29:** 620–628, July 1947.
22. HARDY, SIR W. B.: Microscopic study of freezing of gel. Proc. Roy. Soc., London, s. A. **112:** 47, 1926.
23. MORAN, T.: Freezing of gelatin gel. Proc. Roy. Soc., London, s. A. **112:** 30–46, 1926.
24. STILES, W.: On the cause of cold death of plants. Protoplasma 1930. pp. 459–467.
25. STRUMIA, M.; MCGRAW, J. J.; and REICHEL, J.: Preparation and preservation of human plasma; freezing of plasma and preservation in frozen state. Am. J. Clin. Path. **11:** 388–401, May 1941.
26. HAINES, R. B.: Effect of freezing on bacteria. Proc. Roy. Soc., London, s. B. **124:** 451–463, Jan. 14, 1938.
27. FINN, D. B.: Denaturation of protein in muscle juice by freezing. Proc. Roy. Soc. **111:** 396–411, Sept. 1932.

28. TURNER, T. B.: Preservation of virulent Treponema pallidum and Treponema pertenue in frozen state; with note on preservation of filtrable viruses. J. Exper. Med. **67**: 61–78, Jan. 1938.

29. BREEDIS, C.; BARNES, W. A.; and FURTH, J.: Effect of rate of freezing on transmitting agent of neoplasms of mice. Proc. Soc. Exper. Biol. & Med. **36**: 220–224, Mar. 1937.

30. MIDER, G. B., and MORTON, J. J.: Effect of freezing in vitro on some transplantable mammalian tumors and on normal rat skin. Am. J. Cancer **35**: 502–509, Apr. 1939.

31. KLINKE, J.: Direct proof that cancer and normal cells live after freezing at temperatures down to —263° C. Growth **3**: 169–172, July 1939.

32. GREENE, H. S. N.: Personal communication to G. E. Haggart, Chief of Bone and Joint Surgery, The Lahey Clinic.

33. COLEY, B. L., and HIGINBOTHAM: Use of bank bone in the treatment of central lesions of bone. Papers of the American Association for the Surgery of Trauma, Yorke Publishing Co., Inc., 1949.

34. REYNOLDS, F. C., and OLIVER, D. R.: Exhibit: Merthiolate bone bank. (American Academy of Orthopedic Surgery, 1949.) Washington University, St. Louis, Mo.

35. OLIVER, D. R.: Personal communication.

Osteitis Fibrosa Cystica of the Rib

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PRIMARY tumors of the ribs are rare in contrast to metastatic lesions. All types of primary osseous and cartilaginous growths which affect other bones may be found in the ribs. Harper (*1*) reviewed the literature on primary, benign tumors of the ribs and found only 87 cases; these included 60 chondromas, 11 giant cell tumors, 9 fibromas, and 7 osteomas. He added one case of chondroma and one case of myxomatous degeneration of a chondroma or latent bone cyst that he considered a form of osteitis fibrosa cystica. Schlumberger (*2*) recently reported 67 patients with fibrous dysplasia involving a single bone, 29 of whom had a lesion in a rib.

The diagnosis of a solitary tumor of the rib is often difficult. The history of the patient varies; the patient may complain of pain or may be asymptomatic. Physical examination may be unrevealing as the tumor may not be palpable. A careful search for a primary tumor should be made in all parts of the body. Often, the tumor is discovered when a roentgenogram of the thorax is made. Whenever a tumor of a rib is found it should be considered malignant until proved otherwise. The following examinations should be made: a careful study of the formed elements of the blood; the value of the serum proteins, serum calcium, blood phosphorus, and plasma alkaline phosphatase should be determined; a serologic test for syphilis should be made; and the urine should be tested for Bence-Jones protein. A roentgenologic survey of the skull, vertebrae, pelvis, and long bones to find other tumors is extremely valuable in making a diagnosis. If the results of these examinations are negative, a resection of the rib extending beyond the neoplasm should be performed.

We have studied three patients with isolated rib lesions. In each patient, a diagnosis of osteitis fibrosa cystica or fibrous dysplasia was made.

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CASE REPORTS

Case 1.—The patient, a 19-year-old Negro, was returned from overseas because of a psychoneurosis. He did not have any symptoms referable to his chest, and no tumor was palpated in the thoracic wall. A routine roentgenogram of the thorax (fig. 1*A*) disclosed normal lung fields and a tumor measuring 5 by 2.5 cm. in the right sixth rib in the posterior axillary line. The cortex of the rib was greatly expanded. The central portion of the tumor was radiolucent with numerous, small trabeculations dividing the space into compartments. A roentgenographic skeletal survey was made but no other lesions were found. The laboratory findings were normal.

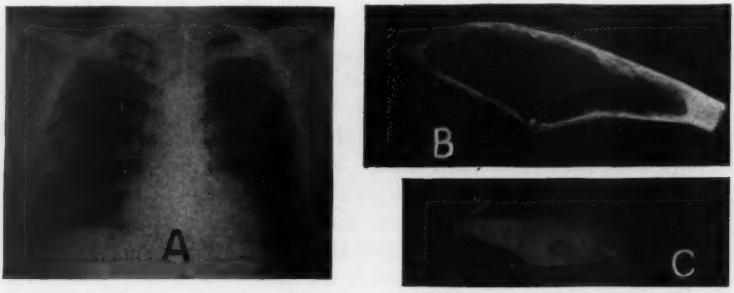

Figure 1.—Case 1. (A) *Roentgenogram of the thorax showing cystic lesion in right sixth rib.* (B) *Roentgenogram of the specimen.* (C) *Longitudinal section of the specimen.*

Thoracotomy, with resection of about 10 cm. of the right sixth rib, including areas beyond the tumor, was performed. The affected rib was exposed in the posterior axillary line and the bone, the adjacent intercostal bundles, and the underlying pleura were explored.

The postoperative course was complicated by subcutaneous emphysema and a small amount of atelectasis in the middle lobe of the right lung and the lower lobe of the left lung. After coughing and expectoration of tenacious sputum, aeration became complete. The wound healed uneventfully.

On gross pathologic examination, the resected portion of the rib was found to be about 10 cm. long. It presented an expansile central portion with a spindle deformity of the rib to about three times the normal diameter (fig. 1*C*). On section, the bone was soft, the cortex thin, and at the greatest diameter looked as though the rib was fractured and partially healed. The central portion of the tumor was occupied by a soft gray mass, and arranged in convolutions about more vascular cores. The tumor was in the expanded central area of the rib and the resection extended beyond the tumor. A roentgenogram of the specimen is shown in figure 1*B*. Microscopic examination of the tumor revealed an intense, loose fibrosis of the medullary spores, with active osteoplasis and no evidence of new bone formation. Foci of osteoplastic giant cells were seen, and in these areas the tissue was slightly more compact and contained numerous polymorphonuclear neutrophils. No evidence of carcinoma was found.

Case 2.—The patient was a 37-year-old white soldier who was transferred to a general hospital with a diagnosis of mild myocarditis. The patient had suffered

a compressive injury of the thorax 19 years previously and had received treatment for a fracture of a rib at that time.

No tumor was palpated in the thoracic wall. No cardiac disease was found. The laboratory findings were normal. A roentgenogram of the thorax (fig. 2*A*) revealed normal lung fields and a large cystic area in the left seventh rib near the posterior axillary line. No destruction of the cortex was seen, but the upper corner of the cortex seemed to be broken, apparently from pressure. A roentgenographic skeletal survey did not reveal any other tumors.

Thoracotomy with resection of about 20 cm. of the left seventh rib was performed. The rib, adjacent intercostal bundles, and the underlying pleura were removed in one mass. The postoperative course of the patient was complicated by an attack of bronchitis that responded to penicillin. The wound healed uneventfully.

The specimen consisted of a segment of rib about 20 cm. long, the center of which was occupied by a spindle-shaped, symmetrically expanding mass (fig. 2*B*). The cortex of the bone seemed to be normal in thickness. The medullary cavity was occupied by a soft, gray-pink mass containing numerous spicules of bone. The gross configuration of the tumor was not remarkable. The tumor filled the expanded portion of bone evenly and extended into the shaft of the bone in both directions. A roentgenogram of the specimen is shown in figure 2*C*. Microscopic examination revealed the marrow cavity to be completely filled with intermingling sheaths of fibroblastic cells having a large number of coagulose processes. There was some evidence of osteolysis and more evidence of the formation of new bone along preexisting trabeculae. Mitoses were not seen. The cortex of the rib was not infiltrated or perforated.

Figure 2.—Case 2. (A) *Roentgenogram of the thorax showing cystic lesion in left seventh rib.* (B) *Longitudinal section of the specimen.* (C) *Roentgenogram of the specimen.*

Case 3.—The patient, a 23-year-old Negro, was returned from overseas because of pain of increasing severity in the anterior portion of the right side of the chest over the costal margin. The pain which was present during rest was aggravated by exercise. A slight, nonproductive cough had been present for about 4 months. The patient had suffered a compressive injury to his chest in an automobile accident about 3 years previously.

Physical examination was essentially normal except for moderate tenderness over the right seventh rib in the anterior axillary line. No tumor was palpated

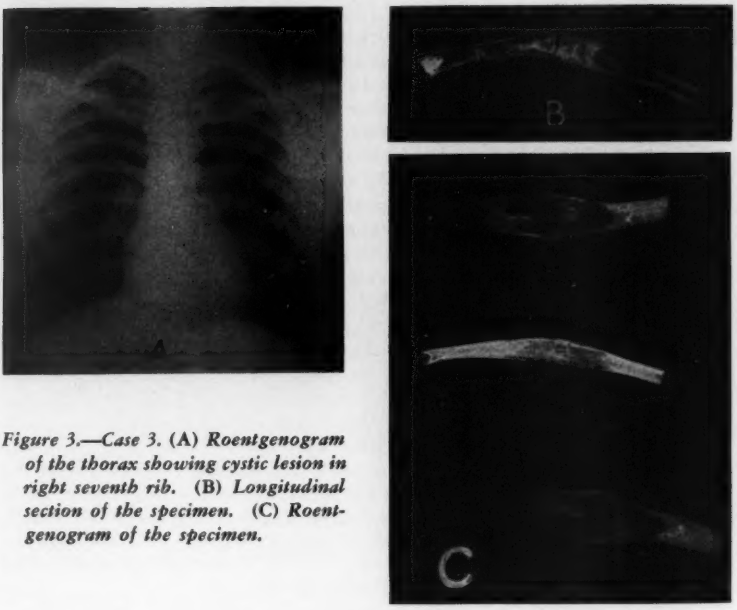

Figure 3.—Case 3. **(A)** *Roentgenogram of the thorax showing cystic lesion in right seventh rib.* **(B)** *Longitudinal section of the specimen.* **(C)** *Roentgenogram of the specimen.*

in the thoracic wall. The laboratory findings were normal. A roentgenogram of the chest revealed normal lung fields and an area of cystic expansion in the right seventh rib in the anterior axillary line (fig. 3*A*). The cortex of the bone around the tumor was thin and numerous, small, fine trabeculations of bone were present within the expanded area. The process seemed rather sharply demarcated and involved a segment of bone about 5 cm. long. No break in the cortex was seen and no soft tissue mass was present. A roentgenologic skeletal survey did not disclose any other tumors.

Thoracotomy with resection of about 12 cm. of the right seventh rib, including an area extending beyond the tumor, the adjacent intercostal muscle bundles, and the underlying pleura was performed. The postoperative course was complicated by a moderate pneumothorax, but reexpansion of the underlying lung was rapid and complete. A slight atelectasis was seen in the lower lobe of the left lung but this cleared rapidly. The wound healed uneventfully.

The resected portion of rib was about 12 cm. long (fig. 3*B*). Near one end and opposite the cartilaginous insertion was a cystic cavity with smooth walls that contained a small amount of clear, yellow fluid. The marrow was fibrous for a distance of about 8 cm. but was otherwise normal. Roentgenograms of the specimen are shown in figure 3*C*). Microscopic examination revealed a loose mat of stellate cells having long processes and separated by a loose, fine, fibrous substance that completely replaced the marrow. Moderate osteolysis and osteoclasis were present. The cortex was thin and the periosteum had an appearance not unlike that of the tumor, but was more compact. No mitoses were found. In the central portion of the mass was a cystic space lined by a thin, flat, single layer of fibroblasts. The surrounding area was composed of compressed tumor stroma in which there were areas of recent hemorrhage. A section taken through

the osteochondral junction showed the medullary lesion to be sharply demarcated from the normal marrow, but the tumor seemed to be present under the periosteum at this point, and extended to the area of cartilage.

DISCUSSION

The three lesions that have been described have no connection with those encountered in the generalized type of osteitis fibrosa cystica caused by adenoma or hyperfunction of the parathyroid glands. The term osteitis fibrosa has been loosely used to refer to all types of bone cyst. With a better understanding of the underlying pathologic changes it has been possible to isolate the particular type of lesion under discussion from the heterogeneous group loosely referred to as osteitis fibrosa cystica. The prime factor in the production of these lesions appears to be trauma. A history of compressive injury to the thorax was obtained in cases 2 and 3.

A consideration of these three lesions reveals that the fundamental changes are those observed in the ordinary repair of bone with a slightly different phase being seen in each case. Geschickter and Copeland (*3*) (*4*) (*5*) have presented the main phases of the problem in their articles on osteitis fibrosa and giant cell tumor. They consider trauma a primary cause of those lesions that arise at a point just beneath injured cortex. The trauma impedes the supply of blood coming from the cortex and produces a subperiosteal hematoma. This factor creates a need for collateral circulation by the medullary cavity to open up new channels in bone for the budding capillaries. The same authors state that this increased osteoclastic activity, in an area where the osteoclasts are already unusually active in the role of new bone construction occurs just at the time when the undernourished cortical bone is undergoing necrosis. Thus an imbalance between bone destruction by osteoclasis and the formation of new bone that would normally proceed from the active cortex is present. Where the defensive reaction of the bone is poor as in the epiphysis, an unchecked hyperplasia of the giant cells occurs and tissue characteristic of a giant cell tumor results. In the metaphysis where the reactive cortical bone is thick and vascular and the tissue reaction can overtake the osteoclasis, an arrested lesion may result which exhibits the various stages of osteitis fibrosa, with and without the formation of cysts. The giant cell tumor of the epiphysis is a lesion in which the healing tendency is not present while the osteitis fibrosa represents an advanced healing stage of bone following trauma. Geschickter and Copeland (*5*) state that a similar reaction may occur in the small or flat bones with the production of a spindle cell variant of a giant cell tumor. Spatial limitations bring the tumor almost immediately into relation with cortical bone on all sides and an early defensive reaction that exhibits itself microscopically as a fibrous proliferation, resulting in a

so-called spindle cell variant of a giant cell tumor, occurs. The tendency toward repair, however, although invoked early, is not so distinct as in the shaft of the long bone where the cortex is thicker and more active. A partial healing process is present.

In osteitis fibrosa, the ordinary bone marrow is replaced by fibrous tissue containing ovoid and spindle cells and, in some cases, many blood vessels. This vascular connective tissue may assume the appearance of ordinary fibrous tissue or have a whorled arrangement. Numerous scattered foci of new bone may be present. Areas of giant cells are found when the proliferative processes are most active. Evidence of hemorrhage may be seen. These findings are those of a healing reaction in bone. Geschickter et al. (*3*) write that varied microscopic appearances, depending on the type of bone affected, the specific site of a long bone involved, and the age of the patient, will be seen.

The roentgenogram of osteitis fibrosa reveals an expansile lesion of the bone marrow with extreme thinning of an intact cortex. The central portion of the tumor is radiolucent with numerous small trabeculae dividing the marrow into compartments.

Having performed the various diagnostic tests enumerated, a differential diagnosis should be attempted. It is assumed that only a single lesion in a rib has been found after a thorough roentgenologic survey. The roentgenologic study will eliminate polyostotic fibrous dysplasia and hyperparathyroidism. A decision may be difficult as to whether a giant cell tumor, a spindle cell variant of the giant cell tumor, or osteitis fibrosa is present, when the diagnosis is limited to these three lesions. The diagnosis can be made only by microscopic study of the tumor, and then if different areas of the same lesion are studied, it may be realized that all of these three conditions, which are different phases of one fundamental process, are being seen.

Statistically, giant cell tumors of the ribs are uncommon. Samson and Haight (*6*) collected only nine cases and added one of their own. It is also difficult to find reports of osteitis fibrosa of ribs since this, too, is an uncommon lesion. This is to be expected since probably the same factor is effective in producing both lesions. An isolated pyogenic abscess of a rib is also an uncommon lesion. Physical examination revealing tenderness over a localized segment of rib, an elevated leukocyte count, with an increased number of polymorphonuclear neutrophils in the peripheral blood stream, and the roentgenogram will indicate the diagnosis.

A gumma may simulate a bone cyst. A positive serologic test for syphilis should make the surgeon suspicious that a syphilitic bone lesion is present. The roentgenogram may reveal a perforation of the expanded cortex, periosteal involvement, and sequestration. Osteo-

mas, osteochondromas, and chondromyxomas may be differentiated by roentgen examination. In many of these cases, however, great difficulty in making an exact diagnosis may be encountered. Eosinophilic granuloma occurs more often in the ribs and skull, although other bones may be affected. Eighty percent of the lesions occur in children. The disease is rarely seen after the age of 25 years. All symptoms are caused by the local lesion but symptoms may be absent. The number and the morphology of the leukocytes are usually normal, although a slight eosinophilia may be present. Values for calcium, phosphorus, and acid and alkaline phosphatase in the serum are normal. On the roentgenogram, a rarefied area with erosion of the cortex and perhaps fracture may be seen. The diagnosis is difficult and removal of a specimen for biopsy or, in the case of a rib, excision may be indicated to obtain material for microscopic study.

A multiple myeloma will usually reveal itself by increased total blood protein values, the presence of Bence-Jones protein in the urine in some, not but all cases, and multiple areas of bone destruction. Instances of myeloma affecting only one bone have been reported but eventually the true nature of the disease will be recognized. A single destructive lesion in a rib may represent a metastatic deposit from a carcinoma elsewhere in the body and a careful roentgenographic survey that includes examination of the pulmonary, gastrointestinal, and genito-urinary tracts, may disclose the primary lesion. In some cases it may be impossible to find the primary lesion on the initial examination. Removal of the affected rib and microscopic examination may reveal a malignancy, although its source may remain unknown for a long time.

Tumors of the intercostal nerves may simulate neoplasms of the ribs both clinically and roentgenologically. Intrathoracic tumors of nerve or tumors of the posterior mediastinum may occasionally be mistaken for neoplasms of the ribs.

Having arrived at a tentative diagnosis the surgeon is confronted with a problem of therapy. If the diagnosis can be definitely established as osteitis fibrosa, there is no need for operation. Mallory (7) states: "There is no record of a case of fibrous dysplasia that was followed by osteogenic sarcoma or other form of malignant tumor, so that there is no probability of harm to the patient if it is left untreated." Since, however, an absolute diagnosis can rarely be made, removal of the affected rib is usually indicated.

SUMMARY

Lesions of osteitis fibrosa cystica of a rib are usually discovered on routine roentgenographic examination of the thorax. A history of trauma to the thorax is obtainable in many instances. The values for

serum calcium, phosphorus, and blood alkaline phosphatase are within normal limits. It is difficult to differentiate the variants of fibrous dysplasia preoperatively. When possible, these lesions should be removed because of the difficulty in making a definite diagnosis. The operative risk is slight.

References

1. Harper, F. R.: Benign chondromas of ribs. J. Thoracic Surg. 9: 132–144, Dec. 1939.
2. Schlumberger, H. G.: Fibrous dysplasia of single bones (monostotic fibrous dysplasia). Mil. Surgeon 99: 504–527, Nov. 1946.
3. Geschickter, C. F.; Copeland, M. M.; and Bloodgood, J. C.: Osteitis fibrosa and giant cell tumor. Arch. Surg. 19: 169–271, Aug. 1929.
4. Geschickter, C. F., and Copeland, M. M.: Tumors of giant cell group; pathologic entity. Arch. Surg. 21: 145–156, July 1930.
5. Geschickter, C. F., and Copeland, M. M.: Tumors of Bone. Revised edition. The American Journal of Cancer, New York, N. Y., 1936.
6. Samson, P. C., and Haight, C.: Giant cell tumor of costal origin. J. A. M. A. 105: 1020–1023, Sept. 28, 1935.
7. Mallory, T. B. (discussant): Case number 32452. (Case Records of the Massachusetts General Hospital section.) New England J. Med. 235: 693–694, Nov. 7, 1946.

An Epidemic of Vomiting and Diarrhea

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DURING the fall and winter of 1948 epidemics of acute gastro-enteritis occurred in the San Antonio area. The disease was characterized by sudden onset of nausea, vomiting, and diarrhea, and was usually accompanied by a low fever. Respiratory symptoms were usually absent. In most patients the course was brief and the symptoms subsided within 24 to 72 hours. In a few patients the fever and symptoms persisted for a week. No sequelae were observed. Since the disease was comparatively mild and of short duration, only a few of the patients consulted a physician and accurate figures on the incidence were not obtained. In this same period the State Health Department of Texas reported a high rate of dysentery. Their cases were probably related to ours since the majority were not confirmed by laboratory findings. Investigation showed that if one member of a family contracted the disease, the other members usually acquired it within the next 3 days. This would suggest a short incubation period, but the syndrome was so widespread and contacts so numerous that no definite conclusions could be drawn.

The syndrome has been variously called "intestinal flu," "virus vomiting and diarrhea," "epidemic diarrhea," "nausea and vomiting," "stomach flu," and "seasonal gastro-enteritis." Because of the wide distribution, the relatively mild character of the symptoms, and the prompt recovery without sequelae, it should be sharply differentiated from so-called "infant diarrhea," the effects of which are often pernicious and prolonged. Clinically, this outbreak corresponded closely to the epidemic of anorexia, malaise, diarrhea, nausea, and vomiting that occurred in October and November of 1943 and 1944 in two boarding schools in Philadelphia (*1*). A series of similar outbreaks occurred in New York City in the fall and winter of 1946–47 (*2*). We have analyzed a series of 13 cases.

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SYMPTOMS

Vomiting, nausea, and anorexia.—Twelve of the thirteen patients exhibited one or more of these symptoms, and it is estimated that about the same proportion holds for the whole group. The onset of vomiting was sudden, was frequently severe and continued for from 8 to 10 hours. The vomitus usually was clear and watery and contained no blood.

Abdominal cramps and diarrhea.—Five of our patients did not exhibit either of these symptoms, and we estimate that this same proportion held for the whole group. When diarrhea occurred, it usually followed the vomiting. The stools were watery, profuse, yellow, and contained no blood or mucus. The responsible agent showed a pronounced tropism for the gastrointestinal tract. The liver and spleen were not enlarged in the patients examined.

Malaise, chills, and weakness.—These symptoms appeared in 11 of the 13 patients. Many also complained of muscular aches, usually in the legs and back during the acute episode. These symptoms prompted the diagnosis of "intestinal flu." A few patients complained of generalized stiffness and soreness associated with general and orbital headaches.

Respiratory symptoms.—These occurred in only 4 of the 13 patients and, when present, varied from a slight serous nasal discharge to a moderately sore throat.

Temperature.—Since few of the patients were hospitalized, temperature charts were not available. Temperatures in those patients whose temperatures were taken were between 99° to 103° F. The fever rarely lasted longer than 24 hours.

LABORATORY FINDINGS

Four patients had a leukocytosis. The percent of polymorphonuclear cells was normal or slightly increased. All of these counts were performed in the first few hours of the disease.

All throat cultures were negative for pathogens. Agglutination-inhibition tests for influenza types A, A′, and B, performed on sera drawn in the acute phase, and 7 to 10 days later, uniformly failed to give a diagnostic rise in titer for any of the strains. Lennette states that in California in 1948 he found proved cases of influenza type A and, simultaneously, cases of vomiting and diarrhea that were negative for known serologic types of influenza (*3*). Agglutinations for *Salmonella schottmülleri*, *Salmonella paratyphi*, and *Brucella abortus* were negative.

One patient gave a cold agglutinin titer of 1 : 128 on the first day of the disease but his convalescent serum was negative. In view of the

fact that he had a respiratory infection a week previously, and that cold agglutinins usually do not appear until five or more days after the onset of primary atypical pneumonia, these agglutinins probably were unrelated to the acute gastrointestinal episode. None of the other patients had significant cold agglutinin titers.

Unfortunately stool specimens were not obtained in a significantly large number of cases. Because of the widespread occurrence of the disease it was not considered to be of bacterial (*Salmonella* or *Shigella*) origin. Bacteriologic studies for enteric pathogens in the cases studied by Reimann and coworkers (*1*) and Gordon et al. (*2*) were negative.

Age.—The ages of our patients (in contrast to diarrhea of the newborn) ranged from 9 to 60 years; but a few cases were reported in younger children and infants. No definite variation in severity was observed in different age groups, but frequently there was variation in severity among the members of a family.

TRANSMISSION EXPERIMENTS

Reimann, Price, and Hodges (*4*) attempted unsuccessfully to isolate a filtrable agent from adults with nausea, vomiting, and diarrhea in the Philadelphia epidemic. Stool supernates were inoculated orally, intranasally, and rectally; pharyngeal washings in bouillon were inoculated intranasally; and Berkefeld (normal) filtrates (both pharyngeal washings and stools) were inoculated intracerebrally in young mice. The results were not significant. These investigators then used the technique of Light and Hodes (*5*) (who had reported isolation of a filtrable agent causing diarrhea in newborn calves from patients with epidemic diarrhea of the newborn), but were unable to duplicate their results. Reimann concluded that perhaps (*a*) the virus had disappeared during preservation of the frozen stools, (*b*) the virus was never present in the stools, (*c*) insufficient amounts of inoculum were used, or (*d*) the disease with which he dealt in the adults was different than that in the newborn.

Later, Reimann, Price, and Hodges (*6*) experimented on human volunteers. Among 32 volunteers who inhaled nebulized filtered garglings, symptoms developed in 17. Of the 21 who inhaled nebulized stool filtrates, 11 developed symptoms. No attacks occurred in 6 volunteers who were fed serum nor in 24 volunteers who were fed serum or filtrates of garglings or stools. The conditions of the experiment were not ideal since isolation of the volunteers was not possible. Furthermore, a declining natural epidemic was present in the population used at the time the experiments were performed. Of the combined groups of 53 volunteers, 28 (53 percent) developed symp-

toms as compared with 22 out of 240 (9 percent) of the remainder of the group studied in which the natural disease apparently occurred during the period of the tests. Reimann and his associates believe that the difference is significant and that the tests suggest that the causative agent of the disease is filtrable, air-borne, enters through the respiratory tract, and is present in the oropharynx, but not in the blood.

Gordon, Ingraham, and Korns (*2*) likewise obtained negative results in experimental animals and successful transmission in human volunteers, but their experience was the reverse of that of Reimann. They were able to transmit the disease without difficulty using stool filtrates administered orally, and were able to transmit the disease by feeding filtered throat washings, but they were unable to duplicate the experiments using nebulized throat sprays of throat washings. Their experiments were well controlled. The incubation period of the experimentally induced disease ranged from 1 to 5 days, compared with 1 to 21 days in Reimann's experiments. Gordon concluded that different etiologic agents were responsible for the disease studied by Reimann, and stated that variations in the epidemiologic and clinical pattern of outbreaks investigated by the State Health Department of New York suggest that gastro-enteritis may be caused by more than one unrecognized agent. This may explain the discrepancies between the respective results, but technical and control factors may be responsible.

Throat washings obtained early in the course of the disease in the San Antonio patients were filtered and administered orally and intranasally to mice with negative results. Filtered throat washings had no effect on embryonated hen's eggs when administered by the yolk sac, amniotic, and allantoic routes. One monkey, fed filtered, bacterially sterile throat washings, developed a transient diarrhea without fever on the second day of inoculation, but the results could not be repeated, nor could the monkey material be passed serially, so that the results were inconclusive. Corneal inoculations of rabbits with throat washings by the technique of Buddingh and Dodd (*7*) were negative.

Through the cooperation of the Department of Preventive Medicine of the University of Texas we attempted transmission experiments in a small series of human volunteers. Five young men were examined thoroughly and found physically normal. None had had a respiratory or gastrointestinal disease within the previous 6 months. After a period of isolation of 3 days, four of these volunteers gargled and then swallowed 5 ml. each of pooled filtered throat washings from two of our patients. The other volunteer was given no inoculum, but stayed in the isolation room with the others. All five were followed

closely for 2 weeks. None showed any symptoms of respiratory or gastrointestinal disease, and their leukocyte counts and temperatures remained normal.

SUMMARY

A widespread epidemic of gastro-enteritis in the San Antonio area was characterized chiefly by sudden onset of nausea and vomiting, often with diarrhea. The disease was self-limited, without sequelae, and recovery usually ensued within 72 hours. Laboratory studies have not revealed the etiologic agent. Attempts to transmit the disease to human volunteers by pharyngeal and oral administration of filtered throat washings were unsuccessful. Because of the close clinical similarity between the patients in this epidemic and others in whom a filterable agent has been shown to be responsible, the syndrome we have described is probably of viral origin.

REFERENCES

1. REIMANN, H. A.; HODGES, J. H.; and PRICE, A. H.: Epidemic diarrhea, nausea and vomiting of unknown cause. J. A. M. A. 127: 1–6, Jan. 6, 1945.
2. GORDON, I. (Albany, N. Y.); INGRAHAM, H. S.; and KORNS, R. F.: Transmission of epidemic gastroenteritis to human volunteers by oral administration of fecal filtrates. J. Exper. Med. 86: 409–422, Nov. 1947.
3. LENNETTE, E. H.: Personal communication.
4. REIMANN, H. A.; PRICE, A. H.; and HODGES, J. H.: Negative results in studies of epidemic diarrhea, nausea and vomiting of unknown cause. Proc. Soc. Exper. Biol. & Med. 55: 233–234, April 1944.
5. LIGHT, J. S., and HODES, H. L.: Studies on epidemic diarrhea of new-born; isolation of filterable agent causing diarrhea in calves. Am. J. Pub. Health. 33: 1451–1454, Dec. 1943.
6. REIMANN, H. A.; PRICE, A. H.; and HODGES, J. H.: Cause of epidemic diarrhea, nausea and vomiting (viral dysentery). Proc. Soc. Exper. Biol. & Med. 59: 8–9, May 1945.
7. BUDDINGH, G. J., and DODD, K.: Stomatitis and diarrhea of infants caused by hitherto unrecognized virus. J. Pediat. 25: 105–113, Aug. 1944.

Cryptococcus Neoformans Meningo-encephalitis

Report of a Fatal Case

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SYSTEMIC fungus disease is not common and consequently is often overlooked, especially in its earliest stages. Furthermore, the isolation of the suspected organism may prove difficult in life and may not be achieved prior to necropsy.

Among the rarest of pathogenic fungi that may lead to fatal infection is *Cryptococcus neoformans*. Up to the present time about 100 cases of cryptococcosis have been reported. This fungus has a particular affinity for the central nervous system. Von Hansemann (*1*) in 1905, was the first to record the lesions of cryptococcosis or torulosis, but it remained for Stoddard and Cutler (*2*) in 1916, first to describe adequately the clinical and pathologic findings. They differentiated infection due to coccidioides, yeast, and *Candida* organisms. Freeman (*3*) presented an excellent histologic study in 1931. A comprehensive review of the clinical features of all cases up to 1937 was reported by Levin (*4*). Reeves et al. (*5*) included the 73 reported cases up to 1941 and added 6 of their own.

A case in which the diagnosis was not definitely established until necropsy is reported.

CASE REPORT

P. I. C., a 42-year-old white man was admitted to the United States Naval Hospital, Bethesda, Md., on 15 October 1948, complaining of recent weight loss, general malaise, headache, nausea, and emesis which began 1 week prior to admission.

He appeared ill and poorly nourished. His initial temperature, pulse, and respiration were normal. The physical examination disclosed only a slight stiffness of the neck and increased muscle tone in the abdomen. The laboratory work, which consisted of a complete blood count, urinalysis, sedimentation rate,

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and serologic studies, showed no abnormality. Five days after admission, he showed personality changes; he was withdrawn and negativistic.

On 5 November, a lumbar puncture was performed, and the cerebrospinal fluid showed xanthochromia, 32 lymphocytes and 95 red cells per cu. mm., a protein level of 1,100 mg. per 100 cc., a decrease in the spinal fluid sugar, and a normal chloride level. The spinal fluid Kahn test and colloidal gold curve were negative. The electro-encephalogram showed a generalized abnormal tracing. A diagnosis of subdural hematoma was considered, and following a neurosurgical consultation, bilateral trephine holes were made on 10 November. No subdural hematoma was found. His recovery following the operation was uneventful.

On 10 December the cerebrospinal fluid revealed xanthochromia, a continued elevated protein, and 29 lymphocytes per cu. mm. No further spinal fluid studies were performed because of the small amount of fluid obtained. The patient received symptomatic care until the middle of January, when he became incontinent of feces and urine. Despite preventive treatment he had decubitus ulcers. Weakness and frequent involuntary movements of the lower extremities occurred, followed later by progressive paralysis of all his extremities. The patient was disoriented, uncooperative, and had frequent hallucinations. His temperature then showed slight elevation.

The clinical impression of meningo-encephalitis of fungal or tuberculous origin could not be substantiated. Further attempts to obtain cerebrospinal fluid were unsuccessful. All previous cultures of spinal fluid had been negative for bacteria and fungi. Throughout his illness the patient showed only transient elevations of temperature, reaching 103° F. on occasion. Starting in November, he was given 100,000 units of penicillin and, except for a few days' interruption, treatment was continued until the latter days of his illness. He received a total of 65 million units of penicillin but his condition did not improve and he died on 6 April 1949, 6 months after the appearance of initial symptoms.

Autopsy

Gross examination.—There were numerous decubitus ulcerations over pressure areas. The skin of the lower extremities was atrophic and edematous. The lungs showed mild congestion. Moderate fatty metamorphosis of the liver was present. In addition there was cystitis and moderate bilateral pyelonephritis.

The brain was normal in size and shape. The leptomeninges appeared cloudy and dull. The convolutions were slightly flattened. There was almost total absence of spinal fluid. The lumbar segment was notably enlarged and softened. The cauda equina was bound in an abundant, gelatinous, grayish exudate. The remainder of the cord, except for dull meninges, appeared normal.

Examination, after formalin fixation, showed that the choroid plexuses of the lateral ventricles were bound with a bulky, grayish, gelatinous, translucent exudate. The remainder of the ependymal lining did not appear involved. The brain substance, including the cerebellum, appeared normal. No cystic lesions were noted in either the meninges or the brain substance. Smears of the exudate in the region of the cauda equina revealed numerous, small, round to oval, single budding organisms.

Microscopic examination.—The meninges and the choroid plexus particularly showed extensive distortion of architecture. The entire structure contained numerous small cystlike areas containing groups of encapsulated organisms lying within giant macrophages (figs. 1, 2, and 3). The organisms were round

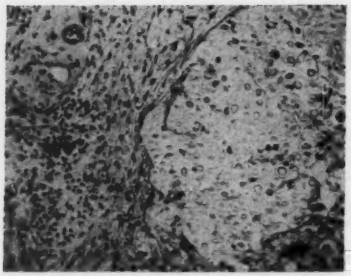

Figure 1.—Sections of the choroid plexus. Note the cystic lesion containing numerous organisms.

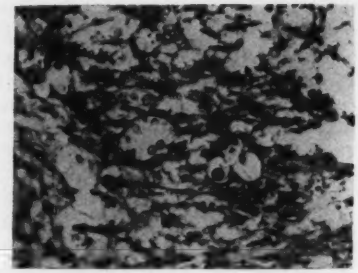

Figure 2.—Sections of the choroid plexus. Note the lack of cellular response to the organisms.

to oval, 3μ to 20μ in diameter, with a thick transparent capsule. The cell body stained lavender with hematoxylin and a brilliant red with periodic acid. Occasional single budding forms were present. Usually several organisms were lying free in the stroma, which was composed of a vascular fibrous tissue containing moderate numbers of lymphocytes and a few monocytes and plasma cells. In general, there was a mild cellular response to the organisms. The adjacent brain tissue showed mild inflammatory changes in the vessels. Representative sections through the cerebral cortex showed slight fibrous thickening of the meninges and a mild infiltrate of lymphocytes and plasma cells. These changes were most pronounced in the sulci. Only an occasional *C. neoformans* was noted here, while the subjacent brain failed to show any. There was mild degeneration of the neurons with some satellitosis.

Spinal cord changes were most noticeable in the lumbar region and about the cauda equina. The leptomeninges were no longer recognizable. The nerve trunks of the cauda were completely ensnared in a dense exudate in which scattered organisms were distinctly outlined by their clear capsular halo. A widespread necrotizing arteritis with edema and cellular infiltration of the wall was present (fig. 4). The tissues immediately surrounding these vessels were necrotic. The neurons and nerve trunks were degenerated and the axons and periaxonal spaces were swollen. The surface of the spinal cord showed severe

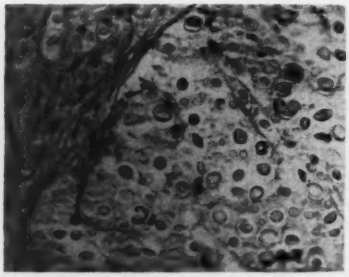

Figure 3.—Details of structure of the organisms. Note the wide transparent capsule.

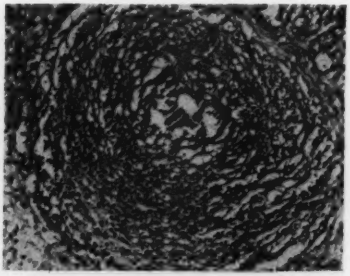

Figure 4.—Sections of spinal meninges. Note the necrotizing arteritis.

edema. There were scattered organisms within the wall. The other tissues showed no evidence of cryptococcal invasion.

The original colonies grew out slowly on Sabouraud's maltose agar, forming round to oval grayish yellow mucoid colonies in which no mycelia were noted. The cells were spherical, encapsulated, and measured 3μ to 12μ in diameter. Intracerebral inoculations of the culture into mice resulted in death; cystic lesions formed which contained myriads of organisms.

DISCUSSION

C. neoformans (*Torula histolytica*) has a world-wide distribution. It has been reported as occurring most often in the southern region of the United States. Benham (*6*) found cryptococci widespread in nature and in both animal and vegetable material; and very frequently found nonpathogenic forms on the skin and in the intestinal tract of normal persons.

The cryptococci are round to oval organisms, 3μ to 20μ in diameter, with a thick transparent capsule demonstrable in tissues or culture. They fail to produce spores or mycelia, either in tissues or culture, and reproduce by a single bud. On initial culture they grow very slowly and produce yeastlike colonies that vary from white to gray or yellow to dark brown. According to Benham the pathogenic cryptococci commonly appear shiny and mucoid. They thrive well on Sabouraud's glucose or maltose agar and subcultures grow quickly, often becoming visible within several days. They are relatively inert biochemically. Most organisms will ferment glucose to form acid, but will usually not produce gas. Intraperitoneal or intracerebral inoculation of saline suspensions of the organism into mice leads to widespread lesions from which the organism may be isolated. Death of the mice commonly occurs in 3 to 4 weeks.

Laboratory examination

From the laboratory standpoint, examination of the blood and urine are of little diagnostic value. The greatest aid comes from examination of the spinal fluid which is often xanthochromic and turbid, although it may be clear. The pressure is usually increased but, in our case, due to involvement of the choroid plexus, fluid production was greatly decreased. The cell count usually ranges from 200 to 800 with wide variation in the extremes and is chiefly composed of lymphocytes. The cryptococci may simulate lymphocytes and have been mistaken for them in the counting chamber. The protein is elevated in both the albumin and globulin fractions (a total of over 1,000 mg. in our patient). The sugar is variable but usually low. The colloidal gold curve is usually of the meningitic type.

Clinical features

In the majority of the reported cases of this disease, the ages ranged from 40 to 60 years; deaths have been reported in a child of 2 and in adults over 70 years.

The disease is slightly more common in men than in women. The portal of entry is not definitely known. The most common route is believed to be via the lungs, although the organisms may enter through the skin, nasopharynx, or gastrointestinal tract. According to Levin (*4*) the organisms have been found in the following organs in order of decreasing frequency: central nervous system, lungs (generalized), kidney, spleen, adrenal, abdominal lymph nodes, the peribronchial lymph nodes, tonsils, subcutaneous tissues, and skin. Almost without exception death has followed involvement of the central nervous system.

The diagnosis is often difficult because (*a*) the disease is uncommon and not always considered in the diagnosis; (*b*) its manifestations are protean so that other more common conditions (the encephalitides and meningitides of tuberculosis, syphilis, other fungus disease, brain abcess or tumor, degenerative neuropathies, and psychogenic disorders) are considered; and (*c*) initial cultures are slow in growth so that the plate may be discarded before the organism has grown out.

Symptoms in our patient simulated psychosis, subdural hematoma, and finally meningo-encephalitis of undetermined origin. In meningeal involvement, common symptoms are headache, dizziness, vertigo, and stiffness of the neck and back. Later, a great variety of mental disturbances may appear. Physical signs commonly suggest a chronic meningitis with stiffness of the neck and back. Other signs include cranial nerve disturbances, papilledema, hyperactive and finally absent deep reflexes, and hemiplegia. Fever commonly is slight or absent, with mild, if any, elevation in pulse rate. Late in the disease, urinary tract and pulmonary infections are frequent complications. The average duration of life after onset of symptoms is from 1 to 6 months, although survival for more than 5 years has been reported.

Differential diagnosis

Tuberculosis and syphilis may be ruled out by appropriate laboratory and clinical examination. Neoplasms and abscesses may provide considerable difficulty. The diagnosis may have to await operation and biopsy. Subdural hematoma may provide considerable difficulty, as in this case.

The chief difficulty may be offered by other mycotic organisms. Those more commonly entering into the differential diagnosis will be

North American blastomycosis, coccidioidomycosis, actinomycosis, moniliasis, and sporotrichosis.

North American blastomycosis is characterized by suppurative and granulomatous lesions especially in the skin, lungs, and bones. In about 30 percent of the patients, central nervous system lesions occur. Like the cryptococcus, it produces a single bud from the parent cell. Unlike the cryptococcus, cultures at room temperature will form mycelia bearing numerous oval to round conidia.

Coccidioidomycosis, in its fulminant form, often ends with terminal dissemination to the central nervous system. The most reliable differentiating feature is the organism itself, which is large (20μ to 80μ in diameter), nonbudding, spherical, and filled with numerous endospores (each 2μ to 5μ in diameter). On Sabouraud's agar at room temperature, aerial mycelial forms are produced. The branching septate hyphae segment into numerous arthrospores. Inoculation into testes of guinea pigs leads to a severe purulent orchitis from which typical organisms containing numerous endospores may be demonstrated.

Actinomycosis may affect the central nervous system but is often preceded by cervicofacial, thoracic, or abdominal suppurative and granulomatous processes that commonly form draining sinuses. In tissues typical colonies of the "ray fungus" may be seen lying in a suppurative area. Gram-negative mycelia are present in tissues and cultures. Pathogenicity may be demonstrated on intraperitoneal injection of guinea pigs.

Moniliasis may occasionally lead to a purulent meningitis with an intense polymorphonuclear and lymphocytic response. The organisms appear as small, oval, thin-walled budding bodies 2μ to 4μ in diameter. In tissues, mycelial elements may or may not be present. Corn meal agar cultures produce mycelia and the characteristic thick-walled, round chlamydospores. Rabbits injected intravenously with *Candida albicans* die in 4 to 5 days and show numerous abscesses in the kidneys.

Sporotrichosis occasionally produces fatal meningitis. There is intense cellular reaction within the meninges, with polymorphonuclear leukocytes and lymphocytes in the spinal fluid. Often the organisms are few and cannot be readily demonstrated. Injection of infected material intraperitoneally into male white rats leads to peritonitis and orchitis. Within the purulent exudate, numerous gram-positive, cigar-shaped intracellular organisms are found. Cultures on Sabouraud's agar at room temperature produce delicate, branching septate hyphae bearing conidia laterally or in groups at the ends of lateral branches.

Treatment

Central nervous system involvement with the *C. neoformans* almost always causes death.

Marshall and Teed (*7*), in 1942, reported recovery in a patient following bilateral mastoidectomy and sulfonamide therapy. Reeves et al. (*5*), in 1941, reported recovery in a patient following sulfapyridine administration. O'Neill et al. (*8*), in 1949, reported recovery in a 49-year-old man following treatment with sulfonamides and autogenous vaccines. However, they claim that no absolute cure can be assured because the disease is chronic and may have spontaneous remissions. Meyer, cited by Conant et al. (*9*), reported that *C. neoformans* is killed in vitro by penicillin in approximately the same dose as is required to kill *Staphylococcus aureus*. Beck and Voyles (*10*) found no beneficial action from the combined use of potassium iodide and sulfadiazine in experimental infection in four species of animals. In our case penicillin in vivo and in vitro had no effect on the organism.

REFERENCES

1. VON HANSEMANN, D.: Ueber eine bisher nicht beobachtete Gehirnerkrankung durch Hefen. Verhandl. d. deutsch. path. Gesellsch. **9**: 21–24, 1905.
2. STODDARD, J. L., and CUTLER, E. C.: Torula infection in man. Monographs of the Rockefeller Institute for Medical Research, No. 6, Jan. 31, 1916.
3. FREEMAN, W.: Torula infection of central nervous system. J. f. Psychol. u. Neurol. **43**: 236–345, Nov. 1931.
4. LEVIN, E. A.: Torula infection of central nervous system. Arch. Int. Med. **59**: 667–684, Apr. 1937.
5. REEVES, D. L.; BUTT, S. M.; and HAMMACK, R. W.: Torula infection of lungs and central nervous system; report of 6 cases with 3 autopsies. Arch. Int. Med. **68**: 57–79, July 1941.
6. BENHAM, R. W.: Cryptococci—their identification by morphology and by serology. J. Infect. Dis. **57**: 255–274, Nov.–Dec. 1935.
7. MARSHALL, M., and TEED, R. W.: Torula histolytica meningoencephalitis; recovery following bilateral mastoidectomy and sulfonamide therapy; preliminary report. J. A. M. A. **120**: 527–529, Oct. 17, 1942.
8. O'NEILL, F. J.; NEWCOMB, A. L.; and NIELSEN, C. S.: Cryptococcus meningitis; report of case. U. S. Nav. M. Bull. **49**: 300–305, Mar.–Apr. 1949.
9. MEYER, cited by CONANT, N. F., ET AL.: Manual of Clinical Mycology. W. B. Saunders Co., Philadelphia, Pa. 1944. p. 125.
10. BECK, E. M., and VOYLES, G. Q.: Systemic infection due to Torula histolytica (Cryptococcus hominis); effect of chemotherapeutic agents in experimentally produced infections. Arch. Int. Med. **77**: 516–525, May 1946.
11. VOYLES, G. Q., and BECK, E. M.: Systemic infection due to Torula histolytica (Cryptococcus hominis); report of 4 cases and review of literature. Arch. Int. Med. **77**: 504–515, May 1946.
12. BUSSE, O.: Ueber Saccharomycosis hominis. Virchows Arch. f. path. Anat. **140**: 23, 1895.

13. FREEMAN, W., and WEIDMAN, F. D.: Cystic blastomycosis of cerebral gray matter, caused by Torula histolytica Stoddard and Cutler. Arch. Neurol. & Psychiat. 9: 589–603, May 1923.
14. MACKIE, T. T.; HUNTER, G. W., III; and WORTH, C. B.: Manual of Tropical Medicine. W. B. Saunders Co., Philadelphia, Pa., 1945. pp. 167–170.
15. MOOK, W. H., and MOORE, M.: Cutaneous torulosis. Arch. Dermat. & Syph. 33: 951–962, June 1936.

Pentothal Sodium Anesthesia for Vaginal Delivery

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WITHIN recent years numerous reports have appeared in the literature describing the advantages and disadvantages of pentothal sodium anesthesia in obstetrics. Most of the favorable reports have been from larger institutions with specially trained anesthesia personnel and special equipment. As a result the charge has frequently been made that pentothal is a satisfactory anesthetic only under these special conditions.

The following series of cases was treated at the obstetrical services of two moderate-sized Army hospitals in Alaska where no special equipment or personnel were available. The original trial of pentothal sodium was made because inhalation anesthesia in the hands of personnel with little or no experience in obstetrical anesthesia was unsatisfactory and a high incidence of respiratory complications in the mothers and depression of the respiration in the babies followed.

The results in the present series were so satisfactory that the authors believe that the experience, under these less than ideal circumstances, may be of some general interest as well as contributing additional information to that already published.

MATERIAL

The patients in this series were dependents of officers and enlisted men and were delivered at either an Army general hospital or an Air Force station hospital, each with a total capacity of about 250 beds.

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A total of 215 vaginal deliveries were done under intravenous pentothal sodium. These were equally divided between primiparas and multiparas (table 1). During the same period 37 deliveries were done under other anesthetics, either drop ether or nitrous oxide, oxygen and ether in closed system, pudendal blocks, local, or under no anesthetic. Pentothal sodium was not used in cases of prematurity or where the need for uterine relaxation was anticipated, as in difficult breech extractions or version. Occasionally, in a patient a satisfactory antecubital vein could not be found. In a few rapid spontaneous deliveries there was time and need only for drop ether analgesia. With these exceptions, intravenous pentothal sodium was used routinely.

Table 1 shows the distribution of cases as to parity and type of delivery. With one exception the breech presentations were frank breeches which crowned out and needed assistance only over the perineum. Pentothal sodium was not used when a difficult delivery, especially with intra-uterine manipulation, was anticipated.

TABLE 1.—*Parity and type of delivery of patients delivered under intravenous pentothal sodium*

	Primipara	Multipara	Total
Spontaneous	26	63	89
Low forceps	65	37	102
Mid forceps	5	0	5
Breech	6	4	10
Modified Scanzoni	4	4	8
Twins	1	0	1
Total	107	108	215

METHOD

The type of analgesia used varied somewhat with the demand of the individual case; however, in the majority of cases the following regimen was used: 0.2 gm. pentobarbital sodium by mouth when discomfort was first experienced; 100 mg. demerol with 0.45 mg. scopolamine by hypodermic when contractions became painful; repeated doses of scopolamine if necessary—but this was the exception rather than the rule. In most cases the patients were not heavily sedated as they entered the second stage.

When a patient was ready for delivery she was taken to the delivery room and the necessary preparations were made before the anesthetic was begun, thus reducing to a minimum the exposure of the infant to the anesthetic. A 2.5-percent solution of pentothal sodium in distilled water was prepared and injected into the antecubital vein without special apparatus except for a short length of rubber tubing interposed between the syringe and the needle.

In one hospital, trained nurse anesthetists were usually available; in the other hospital, medical officers, without previous anesthetic training, administered the anesthetic. A standard gas anesthesia apparatus was always in readiness for the administration of oxygen or inhalation anesthesia if necessary. Blood pressure and pulse were checked frequently.

With the patient in position and ready for the perineal preparation the anesthetic was begun. The solution was injected slowly, 1 or 2 cc. at a time, until the desired level of anesthesia was reached. In most cases the anesthetic was light enough to preserve uterine contractions and in many the patient continued to bear down without excitement. After delivery the patient was maintained in light surgical anesthesia if a repair was necessary. Because of the flexibility of the anesthetic agent and the rapid response it produced, the obstetrician was able to control the level of anesthesia by offering suggestions.

Table 2 shows the amount of pentothal required for multiparas and primiparas. It will be noted that most of the cases required no more than 1 gm. and that a significant number required less than 0.8 gm. Some multiparas needed as little as 0.4 gm. Only 4.6 percent of the primiparas required more than 1 gm.

TABLE 2.—*Amount of pentothal sodium required*

	Number of patients requiring—		
	Less than 0.8 gm.	0.8 to 1.0 gm.	More than 1.0 gm.
Primiparas	30	72	5
Multiparas	38	68	2

RESULTS

Effectiveness of anesthesia—Adequate depth of anesthesia was obtained in all cases. Within one-half to 1 minute after the drug was administered anesthesia was deep enough to permit delivery of the head over the perineum, episiotomy, or application of forceps. With most patients contractions continued without interruption and in many expulsive effort continued without excitement although there was effective analgesia and amnesia and between contractions the patient was asleep. It will be noted in table 1 that 60 percent of multiparous deliveries were spontaneous. This will serve as evidence that contractions and even expulsive effort continued in the majority of multiparas. In primiparas, contractions also continued in the majority of cases although only 24 percent were spontaneous deliveries because of the greater outlet resistance. This is not in accord with

the findings of Hellman et al.[3] and Dippel et al.[4] It seems to us that pentothal is not only a satisfactory anesthetic for spontaneous deliveries but that it made it easy to find and maintain light anesthesia without the excitement and attendant complications so often encountered in inhalation anesthesia.

Only 6 of 215 cases had to be supplemented with another anesthetic. Nitrous oxide and oxygen, with or without ether, was the anesthetic added. Of the 6 cases 1 was supplemented because the needle could not be kept in the vein, 1 because of laryngospasm, 2 because of shallow respirations (these latter 3 will be discussed) and 2 in order to secure uterine relaxation. Thus, the anesthetic effect was considered satisfactory in all but 6 (2.8 percent) of the series.

The attitude of the patients was invariably favorable. They frequently commented on the easy and rapid induction and were surprised to find that they awoke with little or no "hangover." Most patients awoke within 1 hour after delivery and postanesthetic vomiting was present in only a few isolated instances. These factors were especially helpful in our program of early ambulation.

Anesthetic complications—Difficulty was encountered in only 11 of the 215 cases and only 2 of the 11 were serious enough to be considered uncommon regardless of the anesthetic agent.

One patient had laryngospasm soon after induction before there was any stimulation of the perineum or rectum. The spasm was promptly relieved with the administration of oxygen and the introduction of an ordinary airway. Anesthesia was continued with nitrous oxide, oxygen, and ether and the delivery was completed without further event.

One patient had complete apnea for 90 seconds but began to breathe spontaneously and oxygen administered immediately relieved the cyanosis. Anesthetic was continued with gas, oxygen, and ether.

Five patients had shallow respirations but in only one of these cases was it considered necessary to resort to gas, oxygen, and ether. The remainder were carried without further difficulty when oxygen was administered.

Vomiting occurred in only two patients and neither of these aspirated. Both of these patients had vomited prior to the start of the anesthetic.

In two patients increased muscular tonus was observed and caused small tonic spasms of the extremities. This may have been caused

[3] HELLMAN, L. M.; SHETTLES, L. B.; MANAHAN, C. P.; and EASTMAN, N. J.: Sodium pentothal anesthesia in obstetrics. Am. J. Obst. & Gynec. 48: 851–860, Dec. 1944.

[4] DIPPEL, A. L.; HELLMAN, R. J.; WOLTERS, C. E.; WALL, H. A., JR.; and HAIRSTON, F. H.: Sodium pentothal anesthesia for selected vaginal obstetrics. Surg. Gynec. & Obst. 85: 572–582, Nov. 1947.

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by anoxia although in either case respirations were not impaired and no cyanosis was observed. The deliveries were completed under pentothal sodium without difficulty.

Thus anesthetic difficulty was encountered in 11 of the 215 cases (4.9 percent). Only 2 (0.93 percent) of the 215 cases, could be considered serious complications.

There were no remote anesthetic complications. No case of post-anesthetic pneumonia was encountered in this series. There were no maternal deaths.

Fetal complications—Condition of the babies on delivery was classified as: breathed and cried spontaneously, required mild stimulation, and required vigorous stimulation. Mild stimulation consisted of rubbing the back, aspirating the mucus, and an occasional slap on the feet. Vigorous stimulation included administration of oxygen, resuscitation by mouth to mouth breathing (no positive pressure oxygen apparatus was available) and stimulating drugs. The distribution of babies among these classifications shows that 184 (85 percent) breathed and cried spontaneously; 15 (7 percent) were sleepy and required mild stimulation; 12 (6 percent) were significantly depressed; in 4 (1.54 percent) the condition of the baby was not recorded; and 1 (0.46 percent) would not respond.

Among the babies with depressed respiration was one case thought to have intracranial hemorrhage following a difficult breech extraction with the cord wrapped about the neck three times. The child recovered completely and at 6 months was apparently normal.

Among the 216 babies (1 patient delivered twins) there were 6 fetal deaths. Two of these were macerated fetuses known to be dead prior to parturition. There were three anencephalic monsters, an unusual incidence, all of whom were born alive but died shortly after delivery. One baby could not be made to breathe although the fetal heart was heard immediately prior to delivery. Autopsy was not done but the baby appeared normal to external examination. The death could not be fully explained and therefore must be attributed to anesthetic depression. Of the 216 babies there was a gross fetal mortality of 6 (2.8 percent). The corrected mortality was 1 (0.46 percent).

DISCUSSION

The most common objections to the use of intravenous pentothal sodium in vaginal deliveries are the fears of respiratory depression and laryngospasm in the mother and respiratory depression of the baby. We were sufficiently impressed with these points to be wary about introducing this anesthetic in circumstances of limited equipment and personnel. Neither of these fears were materially realized

and we believe that the results presented here are an indication that intravenous pentothal sodium may be used safely in small hospitals with limited facilities provided only that certain reasonable care is employed.

The small incidence of maternal complications can hardly be explained by the fact that relatively small amounts of pentothal were used, for in those few cases where difficulty was encountered, it occurred soon after induction. Rather it appeared that occasionally a patient had some special sensitivity to the anesthetic. Later in the series we adopted the practice of starting inhalation oxygen with the induction and this practically eliminated respiratory difficulty. Stimulation of the perineum seemed to have no tendency to cause laryngospasm as is commonly thought to be the case with stimulation of the anus.

The good result with the babies must be attributed to our effort to keep the time between induction and delivery as short as possible. Although, unfortunately, no specific record of this time was kept, it usually did not exceed 10 minutes. No special effort was made to hurry delivery but rather the anesthetic was not started until all was in readiness for delivery. This is in accordance with the finding of Hellman et al.[5] that the concentration of pentothal in the infant's blood begins to rise appreciably after 9 minutes and soon approximates that of the mother's blood. In those cases of our series where the anesthetic was prolonged prior to delivery, the babies were visibly less alert and responsive but did not constitute a real problem.

The enthusiastic attitude of the patients to the anesthetic, because of the easy and rapid induction and the absence of undesirable aftereffects, was a strong argument for us to continue its use once its safety had been established. We found that the lack of aftereffects helped induce the patients to early ambulation.

In addition to the vaginal deliveries, four cesarean sections were done under intravenous pentothal sodium with considerably less favorable results. All the babies required resuscitation and one, an 8-month premature baby, was particularly slow to respond and died several hours after delivery. The only finding on autopsy was atelectasis. The unduly depressed state of the infants might well be attributed to the larger amounts of pentothal required and the somewhat longer time elapsing from induction to delivery. From this limited experience we believed that pentothal was not a suitable anesthetic for section and, therefore, discontinued its use in such cases.

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[5] HELLMAN, L. M.; SHETTLES, L. B.; and STRAN, H.: Quantitative method for determination of sodium pentothal in blood. J. Biol. Chem. 148: 293–297, May 1943.

CONCLUSIONS

It is our belief that intravenous pentothal sodium is a safe, efficient, pleasant anesthetic for vaginal deliveries, both spontaneous and operative. We believe that it is not indicated in cases of prematurity or when prolonged difficult delivery, especially with intra-uterine manipulation, is anticipated.

SUMMARY

Two hundred and fifteen vaginal deliveries were performed under intravenous pentothal sodium in two Army hospitals in an overseas theater; maternal anesthetic difficulty was encountered in 11 cases, only 2 of which could be considered serious. There were no remote anesthetic complications or maternal deaths; gross fetal mortality was 2.8 percent with a corrected mortality of 0.46 percent.

Eighty-five percent of all babies cried spontaneously and only 6 percent required resuscitation. The absence of undesirable after-effects in the mothers aided in a program of early ambulation.

BIBLIOGRAPHY

1. KASSEBOHM, F. A., and SCHRIEBER, M. J.: Intravenous anesthesia in obstetrics; comparative study of pentothal and evipal soluble with report of 250 cases. Am. J. Surg. **40**: 377–383, May 1938.
2. GREENHILL, J. P.: Anesthesia in obstetrics. Am. J. Obst. & Gynec. **54**: 74–81, July 1947.
3. ALLEN, F. M.: Intravenous obstetrical anesthesia; preliminary report. Am. J. Surg. **70**: 283–290, Dec. 1945.
4. RUCKER, E.: Intravenous anesthesia in obstetrics. Virginia M. Monthly. **70**: 35–37, Jan. 1943.
5. LE BRECQUE, F. C.: Intravenous anesthesia in obstetrics. New England J. Med. **219**: 954, 1938.
6. HELLMAN, L. M.; SHETTLES, L. B.; and STRAN, H.: Quantitative method for determination of sodium pentothal in blood. J. Biol. Chem. **148**: 293–297, May 1943.
7. COOLEY, C. L., and SCHWARZ, H. F.: Sodium pentothal anesthesia in obstetrics. West. J. Surg. **56**: 278–284, May 1948.
8. DREISBACH, R., and SNYDER, F. F.: Effect on fetus of pentobarbital sodium and pentothal sodium. J. Pharmacol. & Exper. Therap. **79**: 250, 1949.

Cyst of the Mandible

Report of a Case With Prosthetic Restoration

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NEOPLASTIC lesions of the mandible often present perplexing problems in surgery and prosthodontia. The oral surgeon and the prosthodontist must work in close cooperation if a satisfactory functional and cosmetic result is to be obtained. The following case report illustrates some of these problems in surgery and operative dentistry.

CASE REPORT

On physical examination in September 1944, the patient, a 22-year-old soldier, was found to have a cyst in the right mandible. This was curetted and he returned to duty but the lesion continued to grow and he was admitted to a general hospital on 30 September 1946 because of a recurrence of this cyst. The lesion was reported as being an eosinophilic granuloma by some and as an adamantinoma by others. The entire right side of the mandible was resected (fig. 1) and later pieces of ilium were used as a bone graft. The bone grafts failed to unite in two places at first but union of the graft with the left half of the mandible was finally obtained; however, nonunion persisted in the middle of the graft. The patient was transferred to Letterman General Hospital where a piece of the left tibia was removed for an osteoperiosteal graft on 3 January 1948. When the right mandible was opened a small pocket of pus was encountered and after curetting the purulent area at the site of nonunion, the wound was closed. The graft was buried in the abdominal wall. On 5 April the osteoperiosteal graft was removed from the abdominal wall and found to be viable. The jaw was opened and the scar tissue was removed from the bone ends. The graft was placed in the area of nonunion and fixed with tantalum wires (fig. 2).

The jaw had been immobilized by a special dental prosthetic splint, but this had to be removed because of erosion of the mucous membranes overlying the ramus of the mandible. Various methods of splinting were tried and the use of the jaw was encouraged in order to stimulate union. It was thought that the patient had enough mandible for good function if a prosthesis could be constructed to immobilize that portion of the jaw. This was accomplished.

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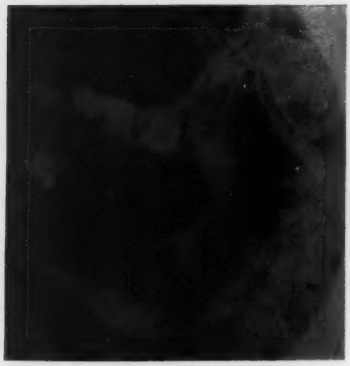

Figure 1.—Roentgenogram showing loss of right side of mandible.

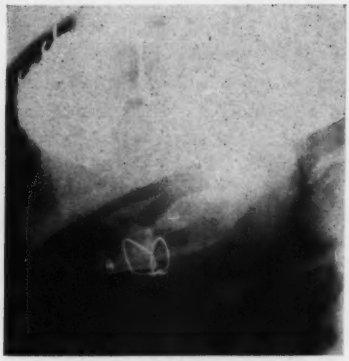

Figure 2.—Roentgenogram showing bone graft fixed by wiring.

Method

Many problems resulted from the unsuccessful attempts to obtain bony union of the bone grafts in this case. The loss of bony structure of the mandible resulted in a shift of the lower jaw of about 8 mm. to the right so that none of the lower teeth were in occlusal contact with the upper teeth (fig. 3). It was necessary, therefore, to use all retention areas on the remaining teeth on the left side and to try to pull the mandible back to the median line. The lower left third molar was tipped lingually to an extreme degree and was partially impacted in soft tissue (fig. 4). The full crown of this tooth was exposed surgically; this tooth was to play an important role in posterior retention of the prosthesis. Following this operation, all necessary operative dentistry was accomplished and two full cast protective crowns for the left lower first and second bicuspids were constructed and additional retention areas were created on these teeth. All the remaining teeth were then treated with sodium fluoride in the hope that maximum protection against further decay in these vitally important anchor teeth could be obtained.

Figure 3.—The position of the lower teeth on closure.

Figure 4.—Linguoversion of the lower left third molar after it had been surgically uncovered.

Figure 5.—Upper and lower castings.

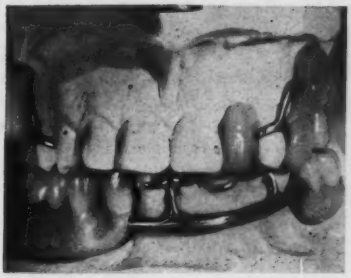

Figure 6.—Labial bar from which clasps and stability were obtained.

Figure 7.—Design of upper appliance.

Figure 8.—Design of lower appliance.

Figure 9.—Position of appliance in the open mouth.

At this point working models were made and the casts were studied to determine the paths of insertion, and all retention areas that were to be used to insure maximum stability were selected. Obtaining a maxillary and mandibular relationship presented an interesting problem in this case because the soft tissue in the right mandibular region would not support bite rims. This problem was met by accepting an arbitrary relationship, obtained by placing the models together in what appeared to be the normal occlusal plane, and then mounting them on the articulator in that position. From this point on, the upper and lower dentures were assembled and fabricated, making certain to keep the upper teeth

on the plane of occlusion desired. When the dentures were inserted, the lower teeth were above the normal plane of occlusion, so they were removed from the denture and the acrylic saddles were trimmed in the outline of base plates without being removed from the gold casting. Bite rims were built on these acrylic saddles and, with the gold casting holding the appliance in its true position, a correct relationship was obtained. The case was then remounted on the articulator, and the lower teeth were reset in occlusion with the upper teeth. The case was then flasked and the lower teeth were processed to the original acrylic saddles.

The upper denture (figs. 5, 6, and 7) was of a simple design, using a modified Kennedy bar with a cast anterior palatal portion, plus combinations of Ackers

Figure 10.—Position of the appliance in the closed mouth.

Figure 11.—Front view of the patient on completion of case.

and Roach clasps. For the lower denture (figs. 5, 6, and 8) a labial and lingual all-around bar was designed to permit the attachment of modified Ackers and Roach clasps and to take advantage of every possible retention area, in the hope that the remaining natural teeth would be sufficient to support the right and free end of the denture which was to rest solely on soft tissue. Following insertion of these dentures no adjustments were required on the gold framework, although several minor adjustments were required around the free-end saddle which was resting on the soft tissue in the right mandibular region. Final results are shown in figures 9, 10, and 11.

SUMMARY

This case presented many problems in view of the fact that all retention for the lower denture had to be obtained from the teeth on the left side, with an extremely tipped left third molar playing an important role. This emphasizes the importance of good roentgenograms, study models, and a thoroughly studied plan before construction of these appliances is begun. Although this patient had only soft tissue as a supporting structure on the right side, the final results were gratifying from both a cosmetic and functional standpoint and when the patient was last seen, better than 70 percent function was observed, and the patient was able to chew soft foods on the right side. Another point of interest was the difficulty in obtaining a true relationship of the maxilla and the mandible; a shift to the right had followed the

loss of bony structure. In view of the fact that the soft tissue on the right side would not support a base plate and bite rims, an arbitrary position was established on the articulator, and the lower partial denture was finished along with the upper partial denture. This procedure permitted observation of the inserted dentures, and an opportunity to determine the approximate relationship in which the teeth should be placed. The cooperation of the patient accounted for a great part of the excellent results obtained. When a successful bone graft is obtained it should be possible to construct an excellent and efficient prosthetic appliance for this patient.

Erythema Exudativum Multiforme (Stevens-Johnson Syndrome)

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ALTHOUGH erythema exudativum multiforme is considered a rare entity, a review of the literature indicates that the condition is more common than previously supposed. Because the average physician is not familiar with this disease it is frequently misdiagnosed. The purpose of this review is to further familiarize physicians and students with the clinical picture and management as an aid to more accurate diagnosis and treatment.

This disease was originally described by Hebra in 1866, by Fiessinger and Rendu in 1916, by Stevens and Johnson in this country in 1922, and by Baader in 1925. Various names for this condition have been used: erythema exudativum multiforme (Hebra); ectodermose erosive pluriorificielle (Fiessinger); a new eruptive fever associated with stomatitis and ophthalmia (Stevens and Johnson), and dermatostomatitis (Baader). Much of the confusion in diagnosis is caused by the multiplicity of names and we believe that the original term used by Hebra is satisfactory and should be adopted.

Erythema exudativum multiforme is an acute systemic disease more common in males. The age incidence seems to be between 22 months and 19 years, although patients over this age have been reported. A group of 54 patients was studied at Duke Hospital by Noojin and Callaway (*1*) who stated, "It is significant that out of the fifty-four selected members not one was a Negro, although there is seen one Negro patient for every three whites at the Medical Clinics of Duke Hospital." It has long been recognized that the disease has a definite seasonal variation, occurring more commonly in the spring and fall seasons. The onset is usually abrupt and characterized by fever ranging from 102° to 106° F. and lesions involving the skin, respiratory tract, and mucous membranes—chiefly those of the conjunctiva, mouth, pharynx, ure-

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thral meatus, and anus. These lesions vary in severity, and in rare instances cutaneous lesions are completely absent.

A distinct cause for this disease has not been proved but the consensus is that the process is a sensitivity reaction of certain persons to any one of a variety of allergens. This may include foods, drugs, and many toxic substances. Howard and Wible (*2*) state, "Nose and throat pathology is undoubtably a greater factor in the etiology of erythema exudativum multiforme than is generally realized." In their series of cases, it was their opinion that half could be directly attributed to sensitization by chronic infection in the tonsils and sinuses and that eradication of these foci was good prophylaxis against repeated attacks. In our series, one patient developed the disease following exposure to embalming fluid while working in a mortuary. He recovered completely and was free from symptoms until October 1948, when he returned home and again worked in a mortuary for the first time since his original attack. In another, it was believed that sulfadiazine was the sensitizing agent; and another was tatooed on the left forearm 1 week before the onset, and it was most interesting to observe that the only cutaneous manifestations in this case were bullous lesions in the area in which the red dye, apparently cinnabar, had been injected. Bacteriological studies on our cases, including throat and conjunctival smears and cultures, revealed only the usual flora of these locations. No inclusion bodies could be found on smear. This conforms with previously expressed opinions that eliminate a specific infection.

In spite of the severity of the disease, when seen in the acute phase, the prognosis regarding life is good, and death is rare. Only five fatal cases have been reported in the literature; in three of these, death was caused by bronchopneumonia (*3*). It should be strongly emphasized that this disease is potentially dangerous to the eye and may result in destruction of sight. Duke-Elder (*4*) believed that in the milder form of erythema exudativum multiforme, the lesions of the eye may heal in a few weeks without scarring, whereas, in the more severe forms the conjunctival lesions may persist for years. In the protracted eye cases, scarring of the bulbar and palpebral conjunctiva frequently results in obliteration of the fornices with corneal opacities and ulcers.

The most important conditions to be considered in the differential diagnosis of erythema exudativum multiforme are drug eruptions, foot-and-mouth disease, pemphigus vulgaris, Vincent's angina, and chickenpox.

Drug eruptions may be difficult to distinguish. The drugs most commonly causing bullous eruptions are sulfonamide compounds, barbiturates, phenolphthalein, iodine, inorganic arsenic, and antipy-

rine. The cutaneous lesions caused by these drugs may simulate the erythema multiformelike eruptions of the skin and mucous membranes, but are not usually as extensive or severe. Oral lesions are rare but have been known to occur. A careful history with special reference to drug ingestion will further help to differentiate the two.

The lesions of foot-and-mouth disease may resemble those of erythema exudativum multiforme, but may be differentiated by the limitation of the cutaneous lesions to the skin near the mucocutaneous junctions and to the fingers and toes. A virus may be demonstrated by guinea pig inoculation in most cases of foot-and-mouth disease.

Although pemphigus vulgaris involves the skin and mucous membranes, it is not too difficult to differentiate it from erythema exudativum multiforme. The onset of pemphigus is gradual, the course is chronic, there is an older age incidence, and tracheobronchial involvement does not occur.

Vincent's angina does not cause bullous lesions on the mucous membranes, skin lesions are absent, and stained smears from the mucous lesions reveal the typical Spirilla or fusiform organisms, or both.

The lesions of chickenpox appear in crops and are smaller than those found in erythema exudativum multiforme. The disease usually runs a mild course and the vesicles dry up in 2 or 3 days.

It has been the authors' privilege to have had under their care nine patients with erythema exudativum multiforme in the past 5 months, all of whom were severely ill and most of them had extensive mucous membrane lesions. All patients responded well to the treatment used and recovered without residual effect. Four of our patients were treated with aureomycin and they will be discussed more fully.

The treatment of this disease comprises local and general measures. In the past, in spite of varied treatment, the average patient recovered rapidly and was free of the disease within 3 or 4 weeks. Because of the severity of the oral and pharyngeal lesions, it is frequently impossible for these patients to take adequate nourishment and liquids by mouth. The general measures adopted in our cases to combat the dehydration and general toxemia included 3,000 to 4,000 cubic centimeters of intravenous fluids daily to which had been added 100 mg. of thiamine chloride, 100 mg. of sodium ascorbate, and 25 mg. of nicotinic acid. In the rare cases with pronounced anemia, blood transfusions are indicated. Crysticillin, 300,000 units, was given intramuscularly every day to combat secondary infection. Two of our patients received sulfadiazine and sulfathiazole (0.5 gm. of each, four times daily). No objective or subjective difference was noted between the patients receiving sulfonamides and those not receiving them. One patient was given crysticillin for the first 3 days; aureomy-

cin then became available and was substituted, 1 gm. orally 3 times daily. Forty-eight hours after the institution of aureomycin the conjunctivitis had resolved by 95 percent. On the eighth hospital day there was 80 percent resolution of the lesions of the penis and on the eleventh hospital day the only lesions remaining were on the under surface of the tongue, the left corner of the mouth, and a very small crust on the foreskin. As a result of the apparent specificity of aureomycin for this condition we were encouraged to follow this form of therapy shortly afterward when three additional cases were admitted within a 48-hour period. Three days after admission aureomycin was begun in a dosage of 1 gm., three times daily. The only other therapy consisted of boric acid eyewashes, hydrogen peroxide mouthwashes, and intravenous fluids. These three patients were excellent for study purposes: one had a mild form of the condition without evidence of vesicles, although he had lesions of the mouth, nose, urethra, and foreskin; the second case was moderate in that in addition to the lesions of the mucous membranes the patient had a few scattered vesicles of the face and chest; the third patient had a severe form of the disease, his entire torso being covered with large bullae. After 8 days of aureomycin therapy we were convinced that this drug was no more effective than the penicillin and sulfonamides had been. There were no complications but the condition in no way responded more rapidly in these patients than in our earlier ones.

Our last patient was admitted following the trial with aureomycin. No therapy, other than boric acid eyewashes, hydrogen peroxide mouthwashes, and intravenous fluids, was given and this patient responded as well as any of the preceding eight.

In the treatment of local lesions strict oral hygiene must be undertaken. A cleansing mouthwash such as one-half strength hydrogen peroxide was used to free the tenacious mucus that accumulated in the mouth and pharynx. The mouth lesions were painted three times per day with 1 percent aqueous gentian violet solution. In cases of extensive involvement with laryngeal lesions and possible obstruction, facilities for emergency tracheotomy or intubation should be available. Weeping and oozing lesions of the scrotum, penis, and skin were treated with boric acid compresses and topical applications of 1 percent gentian violet. The eye lesions are most important and, because of the frequent and dangerous complications, were followed daily by the ophthalmologists. Local measures in the eye consisted of boric acid eyewashes, 30 percent sulfacetimide solution every 6 hours, penicillin ointment every 6 hours, and atropine ointment every 8 hours.

After the acute phase of the disease has subsided a thorough investigation for all foci of infection is recommended as a prophylactic measure against recurrence.

CASE REPORT

An 18-year-old white man entered the hospital on 8 October 1948, complaining of a head and chest cold of 8 days' duration and soreness of the mouth, which began 2 days prior to admission. This illness began while travelling from Florida to San Diego. At the onset, the patient also suffered from headache, inflammation, photophobia, and lacrimation of both eyes, anorexia, and nasal congestion. Shortly after the onset, he began to have attacks of chills and fever, and pains in the chest which were aggravated by severe coughing. Dysphagia began 2 days before admission and burning on urination occurred on the morning of admission.

Past history.—Inquiry into the past history of the patient revealed that he had had a similar attack in 1946, at which time he received penicillin treatment and recovered in 7 days. Prior to the attack he was working in a mortuary. It may be significant to note that while the patient was on leave, just prior to his present attack, he again worked in the mortuary for 1 week.

Physical examination.—Physical examination revealed a well-nourished, young man with a temperature of 103.4° F., pulse 108, respiration 24, and blood pressure 135/80. He was uncomfortable, coughed frequently, and brought up copious amounts of mucopurulent, blood-tinged sputum. Vision was normal, but both bulbar and palpebral conjunctival surfaces were inflamed and drained a mucopurulent discharge. There was no involvement of the sclera. Examination of the mouth disclosed edema of the gingiva, soft palate, and uvula, many areas of inflammation and ulceration of the soft palate and gums, and a thrushlike membrane over the tongue, palate, and buccal mucosa. The lips were fissured and bleeding. Wheezes and rhonchi were heard throughout both lung fields with moist râles in the left base and right midposterior chest. There was slight inflammation of the urinary meatus with a purulent discharge. The skin at this time was normal.

Figure 1.—Bullous lesions of the penis and scrotum.

Figure 2.—Vesicular and bullous lesions of the arms and chest, crusting and fissuring of the lips, and conjunctival involvement.

Figure 3.—Vesicular and bullous lesions of the upper and lower extremities.

On 11 October the scrotum became red and began to itch. Laryngoscopic examination revealed slight swelling in the vallecular region with some difficulty in swallowing saliva. On 12 October a few reddish papules appeared on the right side of the thorax, posteriorly. The urethral discharge had increased considerably and was purulent. The mucous membrane of the glans penis began to slough and large vesicular and bullous lesions appeared over the foreskin and skin of the penis (fig. 1). On 13 October vesicular and bullous lesions appeared on the upper and lower extremities and chest (figs. 2 and 3).

Treatment and hospital course.—The patient was treated with from 3,000 to 4,000 cubic centimeters of intravenous fluids daily, to which had been added 100 mg. of thiamine chloride, 100 mg. of sodium ascorbate, and 25 mg. of nicotinic acid. Crysticillin, 300,000 units and sulfadiazine, 4 gm., were given daily. All oral lesions were painted three times daily with 1 percent gentian violet, and one-half strength hydrogen peroxide was used as a mouthwash. The patient was observed carefully by the ophthalmologist for formation of adhesions of the conjunctivae and for corneal involvement. The eyes were

Figure 4.—Erythema iris type lesions involving the chest and face and hemorrhagic crusting and fissuring of the lips.

treated with boric acid eyewashes which were followed by instillations of sulfacetimide solution every 6 hours. Penicillin ointment was also instilled every 6 hours and atropine ointment every 8 hours. The scrotum and penis were treated with boric acid compresses and 1 percent gentian violet. Vesicular and bullous lesions of the skin were painted daily with 1 percent gentian violet.

Except for a leukocytosis, all laboratory examinations, which included complete blood count, sedimentation rate, urinalysis, and conjunctival smear and cultures, revealed nothing unusual. Biopsy of a skin specimen was consistent with the diagnosis of erythema exudativum multiforme.

The patient's temperature fell to normal on the fifth hospital day and remained normal thereafter. On the eighth day the conjunctivae were 50 percent improved and the lesions of the mouth had regressed so that the patient was able to tolerate soft foods, and the cutaneous lesions were healing rapidly. On the fourteenth hospital day the urethral discharge subsided; and on the thirtieth hospital day all lesions had resolved completely. He was given convalescent leave and upon return was found fit for duty.

Three other patients were treated in a similar manner. Figure 4 shows the appearance of lesions in one of them.

SUMMARY

Erythema exudativum multiforme is more common in the spring and fall months, occurs predominately in males, and is rarely found in Negroes. The disease may be severe, run a self-limited course, is rarely fatal, and recurs. The sites of predilection are skin, respiratory tract, and mucous membranes. The most important sequelae are destruction and scarring of the conjunctiva and cornea, which may in rare cases lead to maceration and ulceration of the cornea with subsequent corneal perforation and panophthalmitis.

Although a definite etiologic factor has not been found, the most likely possibility, in the light of our present knowledge, is a sensitivity reaction.

Except for eye changes, most cases recover regardless of the type of treatment used. General supportive measures are necessary during the acute phase of the illness and we believe that 300,000 units of crysticillin per day was as effective as massive doses of penicillin in combating secondary infection. It was our impression that in the three cases treated with aureomycin there was no specific response. Because of the possibility of severe eye damage, the ophthalmologist should share the responsibility of treatment.

COMMENT

Since completion of this article additional evidence has appeared in the literature (*5*) which seems to indicate a specific viral etiology for erythema exudativum multiforme. We believe that the lack of

response of our cases to aureomycin, which has heretofore been our most effective antiviral drug, does not support this finding.

References

1. Noojin, R. O., and Callaway, J. L.: Erythema multiforme and erythema nodosum; comparative study of 54 patients. Arch. Dermat. & Syph. 54: 560–565, Nov. 1946.
2. Howard, J. C., Jr., and Wible, L. E.: Oropharyngeal manifestations of erythema multiforme. Ann. Otol. Rhin. & Laryng. 55: 146–151, Mar. 1946.
3. Lever, W. F.: Severe erythema multiforme; report of two cases of type ectodermosis erosiva plurorificialis, with development of cicatricial conjunctivitis and keratitis in one case. Arch. Dermat. & Syph. 49: 47–56, Jan. 1944.
4. Duke-Elder, W. S.: Textbook of Ophthalmology. The C. V. Mosby Co., St. Louis, Mo., 1938.
5. Anderson, J. A.; Bolin, V.; Sutow, W.; and Kitto, W.: Virus as possible etiologic agent of erythema multiforme exudativum, bullous type; report of a case. Arch. Dermat. & Syph. 59: 251–262, Mar. 1949.

Bibliography

1. Weisberg, A., and Rosen, E.: Erythema exudativum multiforme. Arch. Dermat. & Syph. 53: 99–106, Feb. 1946.
2. Robinson, H. C.: Erythema multiforme; report of case of severe erythema multiforme with involvement of mucous membranes treated with penicillin. Arch. Dermat. & Syph. 52: 91–92, Aug. 1945.
3. Ageloff, H.: Erythema multiforme bullosum with involvement of mucous membranes of eyes and mouth (Stevens-Johnson disease). New England J. Med. 223: 217–219, Aug. 8, 1940.
4. Shaffer, B., and Morris, P.: Severe erythema multiforme of plurorificalis type (Stevens-Johnson syndrome). J. Pediat. 2: 30, 1948.
5. Soll, S. N.: Eruptive fever with involvement of respiratory tract, conjunctivitis, stomatitis, and balanitis; acute clinical entity, probably of infectious origin, report of 20 cases and review of literature. Arch. Int. Med. 79: 475–500, May 1947.
6. Wright, D. O.; Gold, E. M.; and Jennings, G.: Stevens -Johnson syndrome; report of 9 patients treated with sulfonamide drugs or penicillin. Arch. Int. Med. 79: 510–517, May 1947.
7. Murray, J. O.: Stevens-Johnson syndrome; report of 2 cases. Lancet 1: 328–329, Mar. 15, 1947.
8. Nellen, M.: Stevens-Johnson syndrome; report of case. Lancet 1: 326–327, Mar. 15, 1947.
9. Gray, D. B., and Clair, E. C.: Severe erythema multiforme, (erythema multiforme plurorificialis). West Virginia M. J. 42: 39–41, Feb. 1946.
10. Givner, I., and Ageloff, H.: Stevens-Johnson disease with complete visual recovery. New York State J. Med. 41: 1762–1765, Sept. 1, 1941.
11. Erger, B. D.: Erythema multiforme plurorificialis (Stevens-Johnson disease). Mil. Surgeon 95: 308–312, Oct. 1944.
12. Johnstone, D. F.: Fatal case of Stevens-Johnson syndrome. Lancet. 2: 276–277, Aug. 23, 1947.

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Listerella Monocytogenes Meningitis

Report of a Case

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LISTERELLA MONOCYTOGENES causes an infection in rabbits in which an excess of mononuclear cells in blood is a striking feature. This organism has been recovered from infectious mononucleosis in man and animals, and in meningeal infections in man. Since 1935 when Burn (*1*) first described a case of meningoencephalitis caused by the organism *Listerella monocytogenes*, 24 cases have been reported.

The role of this organism in man and animals has been thoroughly reported by Julianelle (*2*) and more recently by Kaplan (*3*).

Although the disease is relatively rare in man, the mortality rate ranges from 63 to 70 percent (*2*) (*3*). However, with the advent of the sulfonamides, the death rate has greatly decreased. Porter and Hale (*5*) achieved good results by use of sulfanilamide and sulfapyridine in protecting mice from lethal doses of *Listerella*.

Foley, Epstein, and Lee (*4*) found that each of their 7 strains of *Listerella* grew freely in 40 times the concentration of penicillin necessary to completely inhibit the growth of other gram-positive organisms. They therefore assumed that *Listerella* was penicillin-resistant.

In spite of these reports, the strain of *Listerella* recovered in the case reported here was found to be more sensitive to penicillin in vitro than to either sulfadiazine or streptomycin.

CASE REPORT

On 19 May 1949, a 32-year-old white man was admitted to a naval hospital complaining of a severe headache of 14 hours' duration. On admission he was delirious.

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According to his wife, he was apparently well the day prior to admission and he had worked the entire day at his job as a metal die caster. After a large dinner he took a nap for about 1 hour. When he awoke he complained of a slight headache and went to bed.

At 2300 the patient was restless and his temperature was 104° F. A physician gave him an injection of penicillin and he was hospitalized.

The past and family histories were noncontributory.

Physical examination revealed an acutely and seriously ill man. The temperature was 104° F.; pulse, 80; respirations, 20; and blood pressure, 154/84. The neck was stiff, and Kernig's sign was positive, while Brudzinski's sign was negative. The general physical examination was otherwise essentially normal. Complete neurological examination (as far as the cooperation of the patient permitted) was normal except for a positive Babinski reflex on the left.

A spinal puncture, performed soon after admission, showed a pressure of 340 mm. water. The pressure was slowly reduced to 200 mm. water. The spinal fluid was slightly turbid and smears revealed many small gram-positive rods.

Thirty minutes following the spinal puncture the patient's sensorium cleared considerably and the headache was definitely relieved. Fourteen hours after admission severe headache accompanied by delirium returned and a spinal puncture was again performed. At this time the spinal fluid pressure was 520 mm. water, and the fluid was definitely cloudy. The pressure was again reduced to 200 mm. water with immediate relief of symptoms; the blood pressure, which had risen to 180/120 prior to the second spinal puncture, returned to normal.

One more therapeutic spinal puncture was necessary to relieve the headache the following day, 38 hours after admission. The spinal fluid pressure at this time was 190 mm. water, and the fluid was still cloudy.

A 48-hour culture of the spinal fluid showed small gram-positive rods in pure culture. Blood cultures taken on admission were negative. On the third hospital day a specific diagnosis of *Listerella monocytogenes* meningitis was made.

During the next 7 days, repeat spinal punctures were performed for penicillin, sulfadiazine, and streptomycin levels as well as spinal fluid chemistry. Throughout this period, the temperature was returning to normal by lysis and the patient was relatively asymptomatic. On the ninth day of hospitalization the patient had a generalized, follicular, morbilliform type of skin eruption, which responded promptly to antihistaminic drugs and the discontinuation of sulfadiazine and streptomycin. (In vitro studies were now available showing the organism more sensitive to penicillin than to either sulfadiazine or streptomycin.)

The remainder of the hospital course was unremarkable. Penicillin was gradually decreased, and discontinued at the time of discharge on 11 June 1949, 23 days after admission.

Follow-up studies at monthly intervals have failed to reveal any abnormalities in the electrocardiogram, blood, urine, or spinal fluid.

Laboratory findings

Complete red and white blood cell counts after 20 May 1949 were within normal limits. The results of the Davidsohn test, blood Kahn test, and the test for cold agglutinins were within normal limits.

Bacteriology

The organisms were small gram-positive rods, approximately 0.5μ in breadth and 1 to 2μ in length. They were nonencapsulated, and non-spore-bearing. They

appeared singly, in V-shaped pairs, and in chains. Colonies on blood agar were small, transparent, and produced hemolytic zones about each colony. They were sluggish to nonmotile at incubator temperature, but actively motile at room temperature.

Carbohydrate fermentation

Acid with no gas.—Dextrose, 4½ hours; salicin, 4½ hours; levulose, 11 hours; rhamnose, 16 hours; maltose, 16 hours; lactose, 16 hours; and sucrose, 16 hours.

Neither acid nor gas with mannitol, dulcitol, and inulin.

Gelatin not liquefied.

Semisolid media

Growth confined to the line of inoculation with a branching out at the end of 24 hours to give a brush effect.

Indole and hydrogen sulfide negative.

Sensitivity studies

Penicillin.—Presumptive test showed distinct penicillin sensitivity. Tube test revealed the organism to be sensitive between 0.09 and 0.19 unit per cubic centimeter.

Streptomycin.—Presumptive test showed only slight streptomycin sensitivity. Tube test was not done.

Sulfadiazine.—Presumptive test showed distinct sensitivity in 100 mg. percent solution. Tube test showed the organism to be resistant in over 20 mg. percent.

ANIMAL PATHOLOGY

On 27 May 1947, a 7-month-old rabbit was inoculated with approximately 250,000,000 living organisms per cubic centimeter intravenously. The rabbit had an immediate chill, but there was no significant change in either white blood cell count or differential count. The rabbit died about 12 hours later.

On autopsy the organs were grossly unremarkable, except for the liver which was evenly studded throughout with myriads of miliary abscesses, the lungs which showed extreme passive congestion, and the spleen which was enlarged and extremely soft.

Microscopic examination: In the lungs the majority of the alveoli were distended with edematous fluid and contained a few mononuclear cells. In some areas the alveoli were collapsed and airless. The vascular spaces were congested, and red blood cells were observed in the alveolar spaces. Throughout the liver numerous small abscesses were seen. These abscesses had no relation to lobular architecture. The central veins were slightly dilated, and there was some compression of the liver cords. Throughout the adrenals a few small abscesses similar to those seen in the liver were observed. In some areas there was vascular congestion. The kidneys also showed small abscesses within which were seen short, plump, basophilic rods.

Treatment

Emergency treatment was directed toward the reduction of spinal fluid pressure in order to relieve the headache and delirium.

Chemotherapy was begun following the initial spinal puncture, and consisted of the administration of 1 million units of crystalline penicillin, intramuscularly, every 2 hours; streptomycin, 2 gm., intramuscularly, daily; and sodium sulfadiazine, 4 gm. initially, intravenously, followed by 1 gm. orally, every 4 hours thereafter.

On the third hospital day the dosage of crystalline penicillin was reduced to 1 million units every 4 hours, and 300,000 units of wycillin was given every 8 hours.

In vitro studies done on the fifth hospital day showed that the penicillin concentration in the spinal fluid was barely high enough to control the organism's growth, and on that day 200,000 units of crystalline penicillin was given intrathecally. This was the only intrathecal injection given.

With the occurrence of an allergic skin reaction on the ninth hospital day, sulfadiazine and streptomycin were discontinued. Penicillin was given in the same dosage until the fourteenth hospital day, when crystalline penicillin was stopped. However, wycillin, 300,000 units every 8 hours, begun on the third hospital day, was continued until the day of discharge.

Epidemiology

When the patient became clear mentally, an extensive investigation was initiated to determine the epidemiologic factor involved in this case. The facts uncovered were meager. Two weeks prior to his illness a pet groundhog had been kept in his garage. The pet had become ill and was killed and buried by another member of the family; the patient had had no contact with the pet for weeks. The only unusual food was eaten 6 hours prior to his illness, and consisted of frozen African crayfish tails. Other members of the family had also eaten this food with no ill effects.

The source of infection in man is obscure, and the animal reservoir, if such exists, has not been demonstrated.

References

1. Burn, C. G.: Clinical and pathological features of infection caused by new pathogen of genus Listerella. Am. J. Path. **12**: 341–348, May 1936.
2. Julianelle, L. A.: Function of Listerella in infection. Ann. Int. Med. **14**: 608–620, Oct. 1940.
3. Kaplan, M. M.: Listerellosis. New England J. Med. **232**: 755–759, June 28, 1945.
4. Foley, E. J.; Epstein, J. A.; and Lee, S. W.: Effectiveness of penicillin on Listerella. J. Bact. **47**: 110–111, Jan. 1944.
5. Porter, J. R., and Hale, W. M.: Effect of sulfanilamide and sulfapyridine on experimental infections with Listerella and Erysipelothrix in mice. Proc. Soc. Exper. Biol. & Med. **42**: 47–50, Oct. 1939.

The Retromolar Area

Its Significance in Full and Partial Denture Construction

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THE pear-shaped pad of tissue lying distally from the position of the mandibular third molar and formed by the external and internal oblique lines has been known variously as the retromolar area, retromolar triangle, retromolar papilla, or retromolar pad. The importance of this pad of tissue with its underlying structures and its relation to full and partial denture construction has frequently been overlooked. The failure to include this pad of tissue in the mandibular impression, or cutting the resulting impression of this pad from the distal extension of the finished mandibular full or partial denture, will result in early destruction of the mandibular alveolar ridge. This destruction is accompanied by loss of retention, stability, centric relation, vertical dimension, and comfort.

The retromolar pad consists principally of loose connective tissue, within which are located the retromolar mucous glands (*1*). Below the pad are the terminal fibers of the temporal muscle which forms part of the retromolar area (*2*), the pterygomandibular raphe, and that part of the buccinator muscle which arises from the raphe (*3*). Below these structures is the thick periosteum covering the floor of the retromolar fossa (*1*). The bone is of the cortical type, forming a thick band distally from the third molar alveolus. It is functionally active in furnishing attachment for muscles and is, therefore, a relatively stable bone (*4*).

The soft character of the mucosa with the resilient character of the fibrous attachments in the submucosa make this pad of tissue ideal for post dam. This post dam is important in mandibular full denture retention. The dense bone below these structures affords support for the mandibular full or partial denture and resists the forces of mastication.

Anteriorly to the retromolar area, the crest of the residual alveolar ridge is covered with dense fibrous connective tissue (*5*). Below this

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is a thin layer of cortical bone and varying amounts of spongy bone where atrophic changes are common (*1*). The character of the tissue and bone anterior to the retromolar area predisposes to failure of the denture if terminated in this area (fig. 1). Four cases are presented where the partial or full denture failed because it terminated anteriorly to the retromolar pad.

Some factors, such as clasp design, that may contribute to the failure of the partial denture are shown in the illustrations. These factors will not be discussed in this article.

Figure 1.—At **A** *(retromolar area) bone is of the dense cortical type. Partial and full dentures should terminate here. At* **B**, *bone is of the thin cortical and spongy type. Atrophic changes are common under stress if the denture is terminated here.*

CASE REPORTS

Case 1.—The patient had been wearing a maxillary full denture and a mandibular lingual bar partial denture for about a year. His chief complaint was that his anterior alveolar ridge was sore and that he could not masticate his food properly.

Examination revealed an inflamed mucosa under the denture in the maxillary central and lateral incisor area. There was loss of occlusion in the molar area and a ½-mm. space between the teeth. The saddles of the mandibular partial denture did not include the retromolar area. The mandibular alveolar ridge in the molar region revealed apparent absorption of the supporting bone.

Failure to include the retromolar area in the saddles of the mandibular partial denture (fig. 2) had caused the forces of occlusion to absorb the alveolar bone

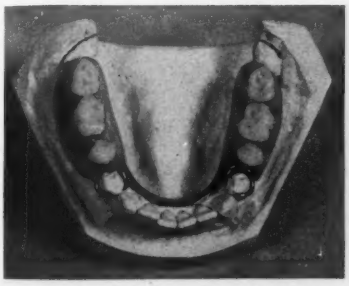

Figure 2.—Case 1. Mandibular partial denture with saddles short of the retromolar area.

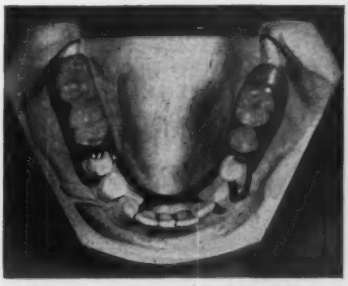

Figure 3.—Case 2. Mandibular partial denture with saddles short of the retromolar area.

resulting in a loss of vertical dimension and discomfort in the anterior maxillary region.

A redesigned partial denture was constructed with extension of the saddles into the retromolar area with correct centric and vertical dimension.

Case 2.—The patient had been wearing a mandibular lingual bar partial denture for 3 months.

His chief complaint was that his mouth was sore, and that excessive amounts of food got under the partial denture. He had had several adjustments during the 3-month period, but did not obtain relief.

Examination revealed the teeth in the partial denture set up in cross-bite relation. The tissue-bearing area of the saddles was small and appeared to be far less than the patient could tolerate. The retromolar area was not included in the saddle (fig. 3).

The partial denture was ill-fitting because of cross bite and inadequate saddles.

A new partial denture was constructed which corrected the cross bite, extended the saddles into the retromolar area, and which enlarged the tissue-bearing area to the tolerable limits of the muscle attachments. This new partial denture has now been worn 26 months with the masticatory function satisfactorily restored.

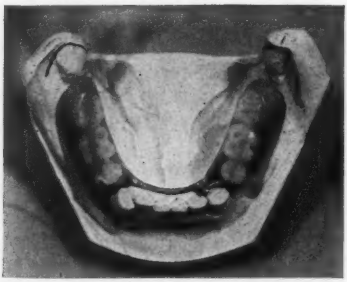

Figure 4.—Case 3. Partial denture in place on stone cast.

Figure 5.—Case 3. Dark lines indicate retromolar area. Broken lines indicate denture area where extensive destruction of the alveolar ridge was apparent.

Case 3.—The patient was wearing a maxillary full denture and a mandibular lingual bar partial denture. While removing the denture, he accidentally severed a blood vessel in the floor of the mouth with one of the clasps. He was referred to the Prosthetic Department for a new prosthetic appliance.

Examination of the mandibular alveolar ridge revealed extensive destruction of the supporting bone. The retromolar area had not been included in the denture area (figs. 4 and 5). There was definite loss in vertical dimension and centric relation.

A new maxillary full denture and a new mandibular partial denture extending the saddles into the retromolar area was constructed.

Case 4.—The patient was wearing full maxillary and mandibular dentures. He stated that his mandibular denture was "very loose." About 1 month previously he had had both maxillary and mandibular dentures rebased to improve their retention.

Examination revealed that the maxillary denture was satisfactory. The mandibular denture had no retention; the tissue-bearing area in the posterior of the right and left sides was inadequate, and did not include the retromolar area (fig. 6). The vertical dimension and centric relation were satisfactory.

The mandibular denture was rebased, extending the tissue-bearing area to the tolerable limits of the muscle attachments and over the retromolar area. This denture has been worn satisfactorily for a year.

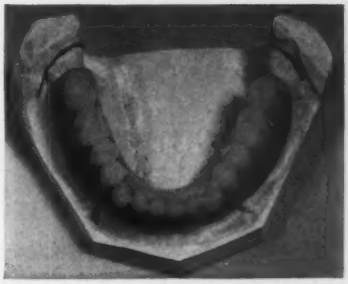

Figure 6.—Case 4. Mandibular full denture with saddles short of the retromolar area.

SUMMARY

Four cases are presented in which partial or full dentures failed. In the cases presented, the dentures failed in the loss of retention, stability, centric relation, vertical dimension, and comfort because the retromolar area was not included in the denture area. The importance of the retromolar area in full and partial denture construction should not be overlooked.

REFERENCES

1. PENDLETON, E. C.: Influence of biologic factors in retention of artificial dentures. J. Am. Dent. A. **23**: 1248, July 1936.
2. HARRIS, H. L.: Anatomy of mouth and its relation to upper and lower full denture construction. J. Am. Dent. A. **18**: 1220–1226, July 1931.
3. EDWARDS, L. F., and BOUCHER, C. O.: Anatomy of mouth in relation to complete dentures. J. Am. Dent. A. **29**: 331–345, Mar. 1942.
4. SWANSON, J. H.: Retromolar area and its relation to adjacent structures. J. Am. Dent. A. **29**: 44–49, Jan. 1942.
5. PENDLETON, E. C.: Minute anatomy of denture bearing area. J. Am. Dent. A. **21**: 488–504, Mar. 1934.

The Hanger Cephalin Cholesterol Flocculation Test and the Maclagan Thymol Turbidity Test

Correlation With Autopsy Findings

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THE cephalin cholesterol flocculation and the thymol turbidity tests have many clinical advantages in determining the extent of liver damage and the differentiation of its various forms. Actually these reactions do not test any known function of the liver and should more properly be regarded as indicators of disturbed liver metabolism rather than as specific liver function tests (*1*).

The more recently described reaction, the thymol turbidity test, was first reported in 1944 by Maclagan (*2*) when "in the course of work on the serum colloidal gold reaction it was noted that the thymol which was used to inhibit the growth of mold in the barbitone buffer produced a marked turbidity or precipitate with certain sera, usually those from patients who had parenchymatous liver disease." Making use of these observations, he devised the thymol turbidity test as "an indicator of liver dysfunction." In a series of clinical cases he determined that this test was about 91 percent reliable in infectious hepatitis and about 52 percent reliable in Weil's disease.

At first it was supposed that the underlying mechanism of these two tests was the same. However, as more clinical cases were studied, many instances were found in which these tests were not at all in agreement or in which they agreed in only certain stages of the disease (*3*). The variation in different stages of the same disease is perhaps best illustrated in infectious hepatitis where the cephalin cholesterol flocculation test becomes abnormal first and the thymol turbidity test remains positive long after the cephalin cholesterol flocculation test has returned to normal (*4*).

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Many investigators, among them Recant, Chargaff and Hanger (*5*), Cohen and Thompson (*6*), and Kunkel and Hoagland (*4*), have proved that, biochemically, the mechanisms of these tests are not the same. Electrophoretically, an increased gamma globulin was found in all sera showing a positive thymol turbidity test, as had previously been shown in cases with an abnormal cephalin cholesterol flocculation test. Immunological methods have failed to demonstrate a qualitative abnormality of this gamma globulin even though the high gamma globulin present in multiple myeloma does not produce a positive thymol turbidity test. It is apparent that both of these tests depend on the gamma globulin content of the serum but in different fashions not yet fully investigated nor understood.

The degree of elevation of the thymol turbidity test appears to be directly proportional to the degree of lipemia present, and the extraction of all lipids from a positive sera prevents the reaction, which can again be made positive by the addition of lipids from a normal serum. Thus, it is believed that in the thymol turbidity test the gamma globulin determines whether the reaction will be normal or abnormal, while the lipemia present determines the elevation of the test. This perhaps explains why no correlation has been found between the severity of symptoms and the degree of elevation of the thymol turbidity test (*7*).

Also, unlike the cephalin cholesterol flocculation test, it has been noted that the thymol turbidity test decreased in liver disease following the intravenous administration of large amounts of concentrated serum albumin over a period of days (*7*). This has been confirmed in various laboratories where an elevation of the serum albumin decreased the thymol turbidity reaction (*4*).

Some of the advantages claimed for the thymol turbidity test are as follows:

(*a*) An easier reagent to prepare with weighed amounts of chemicals which do not require aging.

(*b*) A more stable and less photosensitive agent than the cephalin cholesterol.

(*c*) A satisfactory test that can be performed on sera after several weeks' refrigeration.

(*d*) The results on nonfasting specimens are slightly higher than on fasting specimens but less in error than the cephalin cholesterol flocculation test.

(*e*) An accurate and reproducible result free from subjective estimation and error.

(*f*) A rapid determination; completed in ½ hour instead of 48 hours.

(*g*) Fewer false positive reactions.

(*h*) Appears to be more often normal in uncomplicated obstructive jaundice than the cephalin cholesterol flocculation test.

(*i*) A test of definitely more diagnostic value in following convalescent cases of infectious hepatitis.

(*j*) A test that is easily checked since it is normally elevated in dogs and rabbits.

The emphasis placed upon these 2 tests of liver dysfunction is apparent in the more than 200 articles published in the past 10 years. The clinical and biochemical aspects have been and are being extensively investigated.

The authors of this article believed that a correlation of these tests should be attempted in which not the clinical but the autopsy diagnoses are used. The purpose of this article is to present such a correlation.

Case records and autopsy findings at the Cook County Hospital during 1947 and 1948 were reviewed. Of these, 100 cases were found in which pathologic change was noted in the liver and in which cephalin cholesterol flocculation and thymol turbidity tests had been done. In 91 cases, a total protein determination with A/G ratios was also available. The liver disease was not necessarily the cause of death nor the primary disease of the patient and in no case was death due to cholemia.

The average age of the patients was 57 years. The average time interval between performance of these tests and death was 14 days. In four cases, the thymol turbidity test had been elevated previously and was normal just prior to death, while in two cases, the same occurred with the cephalin cholesterol flocculation test. For the purpose of this report, only the last determination prior to death is used.

The cephalin cholesterol flocculation test was performed by the technique of Hanger (*8*) as modified by Neefe and Reinhold (*9*). A flocculation of more than 2+ in 48 hours was considered abnormal.

The thymol turbidity test was performed in accordance with the technique recommended by Maclagan (*1*). A turbidity of over 4 units was considered abnormal. The thymol flocculation test, as suggested by Neefe and Reinhold, was not recorded.

The serum total proteins, albumin and globulin concentrations were determined after the photoelectric method of Kingsley (*10*). The normal range of total serum proteins was taken as 6.5 to 8.0 gm. per 100 cc.; the albumin as 4.0 to 5.5 gm. per 100 cc.; the globulin as 1.5 to 3.4 gm. per 100 cc.

Of these 100 cases, 122 distinct pathologic diagnoses were determined on gross and microscopic examination of the livers. These diagnoses were divided into 12 groups (table 1).

TABLE 1.—*Distribution of the abnormal cephalin cholesterol flocculation and thymol turbidity tests by groups*

Groups	Abnormal CCF [1] only	Abnormal TT [2] only	Both tests abnormal	Neither abnormal	Total cases
Cirrhosis with jaundice	1	9	14	5	29
Cirrhosis without jaundice	0	0	0	1	1
Congested liver	0	0	0	19	19
Fatty liver	1	10	2	0	13
Primary carcinoma of the liver	0	2	2	1	5
Metastatic carcinoma of the liver	1	5	5	5	16
Toxic hepatitis	3	3	6	0	12
Benign biliary obstruction with infection	0	3	1	1	5
Benign biliary obstruction without infection	0	2	0	0	2
Malignant biliary obstruction with infection	1	4	3	0	8
Malignant biliary obstruction without infection	0	4	0	2	6
Miscellaneous	0	2	1	3	6
Total	7	44	34	37	122

[1] Cephalin cholesterol flocculation.
[2] Thymol turbidity.

The groups were arranged to include cases with a variety of specific lesions in which similar liver damage was found at autopsy. Table 2 lists the percentage efficacy of these tests by groups.

TABLE 2.—*The percentage efficacy of the cephalin cholesterol flocculation and thymol turbidity tests alone and together by groups*

Groups	Number of cases	Percentage efficacy of the CCF [1]	Percentage efficacy of the TT [2]	Percentage efficacy of both tests
Cirrhosis with jaundice	29	51.7	79.3	82.7
Cirrhosis without jaundice	1	0	0	0
Congested liver	19	0	0	0
Fatty liver	13	23	92.3	100
Primary carcinoma of the liver	5	0	80	80
Metastatic carcinoma of the liver	16	37.5	62.5	68.7
Toxic hepatitis	12	75	75	100
Benign biliary obstruction with infection	5	0	80	80
Benign biliary obstruction without infection	2	0	100	100
Malignant biliary obstruction with infection	8	12.5	87.5	100
Malignant biliary obstruction without infection	6	0	66.6	66.6
Miscellaneous	6	0	50	50
Average percent efficacy		27.9	63.9	69.6

[1] Cephalin cholesterol flocculation.
[2] Thymol turbidity.

DISCUSSION

The first group is made up of 29 cases of Laënnec's type cirrhosis with jaundice as a result of this disease. No cases of biliary cirrhosis were included in this group, these having been listed under the appropriate causes of obstruction. Since only about 20 percent of the cases of Laënnec's cirrhosis might be expected to develop jaundice and this usually as a preterminal or terminal event, we would anticipate finding distinct pathologic changes in these livers. This was true in all 29 cases. However, in 5 of these cases both tests were

entirely normal, and in only 14 cases were both tests abnormal. If only one test was abnormal it was more likely to be the thymol turbidity by a ratio of 9:1. This same ratio has been reported elsewhere in cases of cirrhosis (*11*). Maclagan originally reported 13 abnormal thymol turbidity tests in 13 cases of cirrhosis while Stillerman (*11*) reported 96 percent reliability of the thymol turbidity test in 48 cases of clinical cirrhosis. Most of the reports in the literature, however, have indicated a percentage reliability of about 70 percent (*3*) (*12*). As can be seen in table 2, the percentage reliability of the thymol turbidity test in our 29 cases of cirrhosis with jaundice was 79.3 percent while the cephalin cholesterol flocculation test was 51.7 percent reliable. Using both tests, one or the other, or both indicated liver disease in 82.7 percent of the cases. Theoretically, we would expect to find a high percentage of reliability of the thymol turbidity test in cirrhosis since all the factors which tend to elevate this test are present. That is, a high gamma globulin, a high lipid, and a low albumin level in the blood (*4*). The explanation of this discrepancy must await further studies on the basic mechanism of this test.

The second group included only one case of cirrhosis without jaundice in which neither test was abnormal.

In the third group were 19 cases of congestion of the liver. These included chronic passive congestion, and congestion occurring in the terminal state. The gross and microscopic findings in the liver were similar to those found in congestive heart failure, although in only one case was this the cause of death. Positive thymol turbidity values have been reported in from 30 to 55 percent of patients suffering from various types of heart disease (*11*) (*13*). That this was not simply the result of congestion of the liver was pointed out when it was noted that the presence or absence of circulatory failure did not appear to influence the results of these tests (*11*). Similarly, in our 19 cases, simple congestion of the liver did not cause either test to be abnormal.

Thirteen cases were diagnosed as fatty infiltration of the liver. This is a stage through which a number of parenchymatous diseases of the liver pass early in their course and from this stage either healing or destructive disease may follow. In the typical case of virus hepatitis, the highest thymol turbidity values are found between the tenth and twentieth days (*12*) of illness, at which time the blood lipid level is also high (*4*) and at which time some fatty infiltration may first be seen in liver biopsies. Our findings in 13 cases of fatty infiltration also showed a high percentage of reliability for the thymol turbidity test (92.3 percent) while the cephalin cholesterol flocculation test which is less affected by blood lipids was only 23 percent reliable in

indicating liver disease. One or both tests were abnormal in all 13 cases.

Five cases of primary carcinoma of the liver were found in which no obstruction was apparent. Four of these (80 percent) had abnormal thymol turbidity values while in all five the cephalin test was normal. The elevated thymol turbidity values could not be correlated with the extent of liver replacement by tumor since an estimated 60 to 80 percent of the liver parenchyma was grossly and microscopically normal in each case. This has also been noted elsewhere (*12*). Stillerman reported that 7 of 15 cases of neoplastic disease had elevated thymol turbidity tests but whether the process was primary in the liver or metastatic is not stated.

Of the 16 cases with metastatic carcinoma of the liver without biliary obstruction, both tests were abnormal in 5, neither test was abnormal in 5, an abnormal thymol turbidity test only was noted in 5, and in 1 case the cephalin test alone was abnormal. Kunkel, working with clinical material, found a number of cases with metastatic neoplasm in the liver which showed abnormal thymol turbidity values and normal cephalin cholesterol flocculation tests. Here again, the abnormal values could not be correlated with the extent of parenchymal destruction.

Toxic hepatitis, more frequently caused by toxicity associated with disease other than that due to drugs or poisons, was evident in 12 cases at autopsy. In three cases the thymol turbidity test alone was abnormal, in three cases the cephalin test alone was abnormal, while in six cases both tests were abnormal. Thus each test was 75 percent reliable and together they indicated disease in all 12 cases. Popper and Franklin (*14*) in studying 21 clinical cases of toxic hepatitis with biopsy specimens, found that most of these cases had abnormal values for the thymol and cephalin tests but found that in a number of cases both tests were normal when considerable damage was indicated by the biopsies and other laboratory tests. Evidence suggests that many acute infectious diseases have an associated toxic hepatitis, for some investigators have reported that as many as 37.5 percent of patients with acute infections have abnormal thymol turbidity tests which return to normal during convalescence (*11*).

Five cases were classified as benign biliary obstruction with infection, and two cases as benign biliary obstruction without infection. In neither group was the cephalin test alone abnormal, while the thymol turbidity test was 80 percent reliable in the presence of infection and 100 percent reliable without infection of the biliary tract. From the literature it might be expected that both tests would be more reliable in the cases of obstruction with infection but our groups here

are quite small and perhaps with a greater number of cases this would be true. The poor correlation of the extent of disease with the cephalin cholesterol flocculation test, and good correlation with the thymol turbidity test, has been observed elsewhere in cases of biliary obstruction (*7*).

Of the 14 cases with malignant biliary obstruction, 8 had associated infection of the biliary tract and 6 were without infection. An abnormal cephalin test alone was noted in only 1 of these 14 cases while in 3 cases with infection both the cephalin and thymol turbidity test were positive. In considering all 21 cases of biliary obstruction together we do find that the thymol turbidity test is about 10 percent more reliable in the presence of infection. Popper and Franklin reported 73 cases of biliary obstruction, 33 of which were due to cancer and 40 were of benign origin. They also noted that most of their cases showed normal cephalin tests while the thymol turbidity test was slightly elevated.

The miscellaneous group included one case of multiple myeloma in which the total proteins were 10.4 gm. per 100 cc. of which 9.2 gm. was globulin. This patient had a normal thymol and cephalin test 1 day prior to death. At autopsy the liver was large and the seat of myelomatous and moderate fatty infiltration. The second case was that of miliary tuberculosis with diffusely scattered tubercles throughout the liver. Here again, both tests were normal. A third case was found to be Hodgkin's disease in which the liver was enlarged and showed a diffuse infiltration of the lymphomatous process.

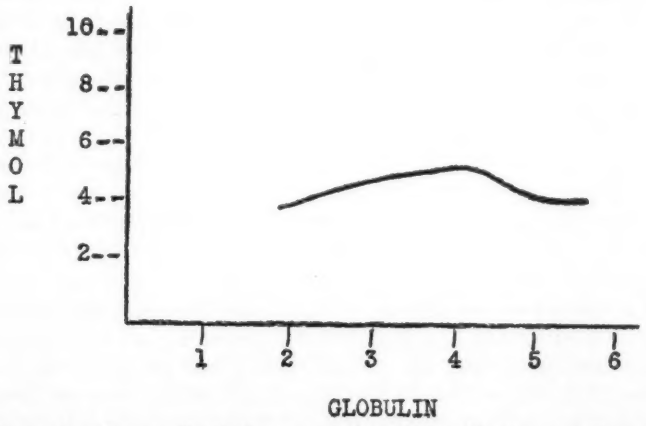

Figure 1.—A mean distribution curve of 91 cases with the mean thymol turbidity value in Maclagan units plotted against the globulin level in the blood in gm. per 100 cc.

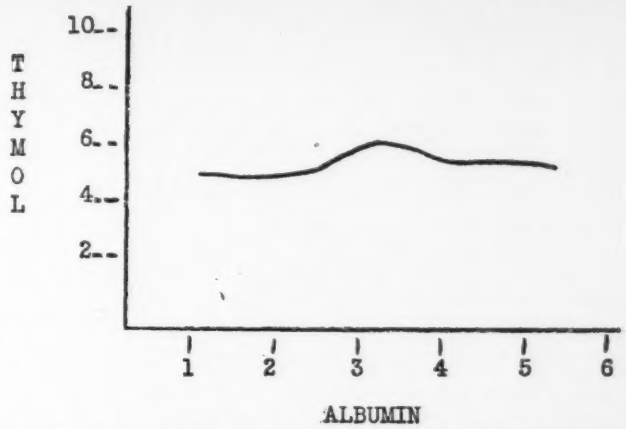

Figure 2.—A mean distribution curve of 91 cases with the mean thymol turbidity values in Maclagan units plotted against the albumin level in the blood in gm. per 100 cc.

In this case the thymol turbidity was 16.8 units and the cephalin test was 4+ in 48 hours. A case of pernicious anemia had an abnormal thymol and normal cephalin test. At autopsy, the liver was found to have a central necrosis of all lobules. One case diagnosed as a reticulum cell carcinoma of the lymphoid tissues had an abnormal thymol and normal cephalin test. The liver was diffusely infiltrated by the carcinomatous disease. The last case was one of nutritional anemia in which both tests were normal. At autopsy, generalized moderate atrophy of the liver cords was noted with an over-all brownish pigmentation and no evidence of regeneration. To determine what relation the thymol turbidity in Maclagan units might have to the globulin level in the blood, a mean distribution curve was prepared (fig. 1). Ernst and Dotti (*12*) found a mean deviation of 1.8 in 522 thymol turbidity values on 500 supposedly normal individuals. While in those suffering from disease not considered to involve the liver, a mean deviation of 2.7 was found in 538 tests on 527 hospitalized patients. Figure 1 has a deviation of less than these observers found in normal subjects and we can conclude that the thymol turbidity test, in units, bears no relation to the total globulin level of the blood. Similarly, when a mean distribution curve is prepared using the albumin level in the blood, no significant deviation is apparent (fig. 2). While therapeutically elevating the albumin level may lower the thymol turbidity reading in an individual case, the initial thymol reading does not appear to be significantly related to the initial albumin level of the blood.

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CONCLUSIONS

A certain error is inherent in our series since in 22 cases there were 2 concurrent pathologic conditions in the liver. However, these were conditions commonly found together and expected in any study of patients with liver disease whether studied from a clinical or pathologic standpoint.

Our correlation of the cephalin cholesterol flocculation and the thymol turbidity test with autopsy findings in the liver is in accord with the clinical work reported in the literature. The thymol test was more than twice as reliable an indicator of liver disease in this series than was the cephalin test but notable discrepancies are apparent so that for maximum reliability both tests must be used.

The thymol turbidity test was found to be highly reliable (92.3 percent) in cases of fatty infiltration of the liver and more reliable in primary (80 percent) than in metastatic (62.5 percent) carcinoma of the liver. In biliary obstruction, it was 75 percent reliable without infection and 85 percent reliable in the presence of biliary tract infection. The thymol test indicated liver disease in about three out of four cases of cirrhosis with jaundice and the same proportion in toxic hepatitis. No abnormal values were found in simple congestion of the liver.

The cephalin cholesterol flocculation test was found to be most reliable in cases of toxic hepatitis (75 percent), cirrhosis with jaundice (51.7 percent), and metastatic carcinoma of the liver (37.5 percent). It was only 23 percent reliable in cases of fatty infiltration as compared to 92.3 percent for the thymol test. Normal values were obtained in primary carcinoma of the liver and generally normal values were noted in all cases of obstruction.

At this point we should like to introduce what we believe to be a new concept of the thymol test. That is, that this so-called test of liver dysfunction may actually be a test that indicates the function of regeneration of the liver in response to disease. The concept of the thymol turbidity test as an index of liver regeneration is not without flaws but does explain some of the following:

(*a*) In virus hepatitis, the thymol test is usually the last test to become abnormal and the last to return to normal. If we consider that the process in the liver proceeds from disease to destruction to regeneration, in that order, with overlapping of these stages, then the period in which the thymol test is abnormal corresponds most closely with the period of regeneration and not with the period of onset or subsidence of liver disease or destruction.

(*b*) Fatty infiltration of the liver is considered by many to be a stage of healing or regeneration and it is in this stage that the highest reliability of the test seems to occur.

(*c*) The thymol turbidity test is abnormal in a significant proportion and frequently a majority of the cases of localized liver disease (such as carcinoma) when there are large areas of normal liver tissue and when other tests of liver function are normal. Perhaps localized regenerative processes about the lesions cause the abnormal thymol test.

(*d*) In overwhelming liver disease sufficient to cause the death of the patient, such as acute yellow atrophy and advanced cirrhosis, the extent of destruction is readily apparent clinically and is indicated by most laboratory tests. Yet in these cases the thymol turbidity test is frequently normal (*3*) and microscopic examination of the liver frequently reveals a notable absence of regeneration. Those who have followed these patients with serial thymol turbidity determinations find that the test is initially abnormal but that as the patient enters the terminal stage, when presumably the power of regeneration has literally been overwhelmed by extensive disease and tissue destruction, then the thymol test returns to normal. We observed this in four case records of patients with advanced cirrhosis in which earlier thymol values were abnormal but the last test prior to death was in the normal range.

SUMMARY

One hundred and twenty-two autopsy diagnoses of liver disease were correlated by groups with the thymol turbidity and cephalin cholesterol flocculation tests and found to be in accord with the clinical results reported in the literature.

In general, the thymol test was twice as reliable as the cephalin test but notable discrepancies occurred.

The use of the thymol turbidity test is suggested as an index of liver regeneration.

REFERENCES

1. MACLAGAN, N. F.: Thymol turbidity test; new indicator of liver dysfunction. Brit. J. Exper. Path. **25**: 234–241, Dec. 1944.
2. MACLAGAN, N. F.: Thymol turbidity test; new indicator of liver dysfunction; preliminary report. Nature, London **154**: 670–671, Nov. 25, 1944.
3. WATSON, C. J., and RAPPAPORT, E. M.: Comparison of results obtained with Hanger cephalin-cholesterol flocculation test and the Maclagan thymol turbidity test in patients with liver disease. J. Lab. & Clin. Med. **30**: 983–991, Dec. 1945.
4. KUNKEL, H. G., and HOAGLAND, C. L.: Mechanism and significance of thymol turbidity test for liver disease. J. Clin. Investigation **26**: 1060–1071, Nov. 1947.

5. RECANT, L.; CHARGAFF, E.; and HANGER, F. M.: Comparison of cephalin-cholesterol flocculation with thymol turbidity test. Proc. Soc. Exper. Biol. & Med. **60**: 245–247, Nov. 1945.
6. COHEN, P. P., and THOMPSON, F. L.: Mechanism of thymol turbidity test. J. Lab. & Clin. Med. **32**: 475–480, May 1947.
7. KUNKEL, H. G.: Value and limitations of thymol turbidity test as index of liver disease. Am. J. Med. **4**: 201–207, Feb. 1948.
8. HANGER, F. M.: Serological differentiation of obstruction from hepatogeneous jaundice by flocculation of cephalin-cholesterol emulsions. J. Clin. Investigation **18**: 261–269, May 1939.
9. NEEFE, J. R., and REINHOLD, J. G.: Photosensitivity as cause of falsely positive cephalin-cholesterol flocculation tests. Science **100**: 83–85, July 28, 1944.
10. KINGSLEY, G. R.: Direct biuret method for determination of serum proteins as applied to photoelectric and visual colorimetry. J. Lab. & Clin. Med. **27**: 840–845, Mar. 1942.
11. STILLERMAN, H. B.: Thymol turbidity test in various diseases. J. Lab. & Clin. Med. **33**: 565–572, May 1948.
12. ERNST, R. G., and DOTTI, L. B.: Evaluation of thymol turbidity test. Am. J. M. Sc. **216**: 316–329, Sept. 1948.
13. CARTER, A. B., and MACLAGAN, N. F.: Some observations on liver function tests in diseases not primarily hepatic. Brit. M. J. **2**: 80–82, July 20, 1946.
14. POPPER, H. (Chicago), and FRANKLIN, M.: Diagnosis of hepatitis by histologic and functional laboratory methods. J. A. M. A. **137**: 230–234, May 15, 1948.

Anterior Fixed Bridges

A Technique for Construction by Means of One-Piece Casting

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THE paucity of literature available on construction of anterior fixed bridges by means of one-piece castings leads to the belief that this method is not in common use. Should this premise be correct, it is regrettable, for bridges constructed by the technic described here have been found to be stronger, easier to seat, and therefore subject the teeth to less torque; in addition, it effects a saving in chair and laboratory time. It is necessary to have only two sittings: the preparations and impressions are made at the first sitting and the completed bridge is inserted at the second.

A detailed discussion of the preparation of the abutment teeth to receive the three-quarter crowns will not be given. However, the preparations must be precise and all surfaces should be made as smooth as possible with sandpaper disks and fine finishing stones. The importance of cutting parallel grooves cannot be overemphasized. The mesial grooves of the abutment teeth must be cut parallel to each other and the distal grooves cut parallel to the mesial. To accomplish this a long-pointed Boley millimeter gage is used; the points are coated with carbon or indelible pencil and the mesial surfaces of both abutment teeth are marked. The mesial grooves are cut and, when completed, the positions of the distal grooves are marked in the same manner, using the mesial grooves as a guide. It follows then that all four grooves must be parallel. This is important in the construction of anterior fixed bridges by any method but is mandatory when using the one-piece casting technic.

A number of impression materials[2] may be used with good results but their preparation for use is not as simple as with some elastic im-

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[2] The material used should not have to be soaked in hardening solution as the change in dimension, after soaking for 15 minutes, is deleterious to the finished model.

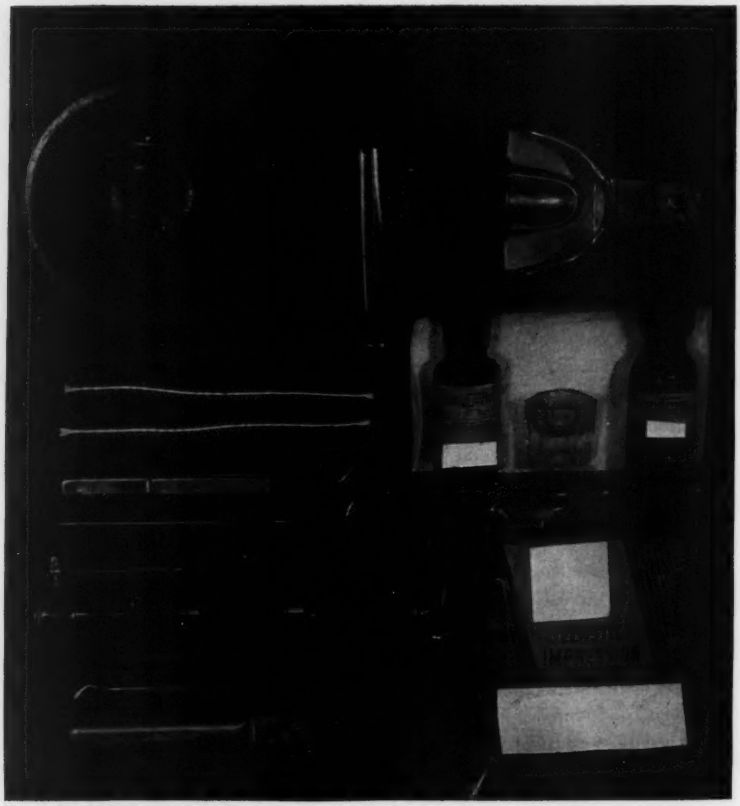

Figure 1.—Equipment required for making impressions.

pression creams. The equipment required for the latter is a rubber bowl, a plaster spatula, cement spatula, a 5-cc. glass or metal syringe and a shortened 18-gage needle (fig. 1).

Prior to taking the impression, the gingival tissue must be pushed back 2 or 3 mm. from the finish line of the preparation. This is accomplished by inserting a piece of string saturated with an astringent (dental glycerite on the Supply Table or a 20-percent solution of zinc chloride) under the free margin of the gingival tissue; the diameter of the string used is comparable to that of a 14-gage wire. The initial insertion of the string is made at a point on the labial surface a few millimeters anterior to the mesial labial wall of the preparation and is gently pushed in place under the mesial, lingual, and distal gingiva with an instrument such as Woodson's No. 2 plastic. Undue trauma must be avoided for it will tear the tissue from its attachment

and prevent return to its normal position. The string is left in place for about 5 minutes and then gently removed. It is important that all bleeding be checked, that the cavity preparation is free from blood and debris, and thoroughly dry or an accurate impression cannot be made.

Impression cream is mixed in 50 cc. of water at 40° F. to allow sufficient time for filling the syringe and inserting the cream under the free margin of the gingiva before the cream begins to harden. The material is carried to the syringe with a cement spatula and is pumped into the barrel. The plunger is inserted and any incapsulated air is forced out. The needle is then attached and the material is inserted under the gingival tissue and over the surfaces of the abutment teeth in a circular motion. When several layers have been deposited, a previously selected tray is filled with the remaining impression material and placed in position. Setting time in the mouth is approximately 5 minutes. When the impression is removed it is carefully examined for air bubbles and if any are found it should be retaken. Saliva is removed by washing in cold water. The impression is then dried with compressed air and without undue delay an artificial stone model is poured by carefully vibrating the material in place. If a vacuum machine is available, its use is recommended before pouring the model.

An impression of the opposing teeth and a registration of the bite is taken in any manner preferred by the individual operator.

Figure 2.

Figure 3.

When setting of the stone model is complete, it is separated and trimmed to remove all surplus material. That part of the model that represents the overhanging free margin of the gingival tissue is carefully removed to permit free access to the finish line of the three-quarter crown preparations of the abutment teeth. At this point the model is further trimmed to receive the necks of previously selected facings and the facings are tentatively arranged in the space to be bridged although no attempt is made to grind them in. The stone model is then immersed in a warm water bath for a period of approximately 5 minutes to prepare it for a duplication. It is next placed in a duplicating flask and the duplicating material is poured. The latter is permitted to set for 1 minute and the flask is immersed in an ice water bath that covers approximately 1 inch of its base and is permitted to chill for 30 minutes. The stone model is next carefully removed and another model is poured, using cristobalite model investment. Upon separation the stone and cristobalite models should be carefully examined to insure that exact duplication has been attained.

To permit free access to the distal surfaces of the abutment teeth for the purpose of contouring the wax three-quarter crowns and for establishing contact points, it is necessary to split the cristobalite model into three sections. This is accomplished by first trimming and beveling the base of the model and scouring its under surface. The

base is well-lubricated and set on a mix of plaster of paris to establish a matrix which will receive the pieces of the cristobalite model after splitting. Starting at the base of the model, saw cuts are made at points that approximate the distal interproximal spaces of the abutment teeth. The cuts are brought to within a few millimeters of these spaces and the model is fractured by inserting a blade of a knife or some suitable instrument (figs. 2 and 3).

The case is now ready for waxing of the three-quarter crowns and for this purpose, the use of a pair of blunt-end pliers of the type used for removing cotton has proved ideal. If the pliers are not overheated, the wax can be carried to the model and the flow kept constantly under control. Trimming and shaping the wax pattern may be accomplished by any means suitable to the operator except that the margins must not be touched with a sharp instrument. For this purpose a heated explorer is used and the excess wax is carefully burnished off. Any instrument that will cut or scrape wax will also

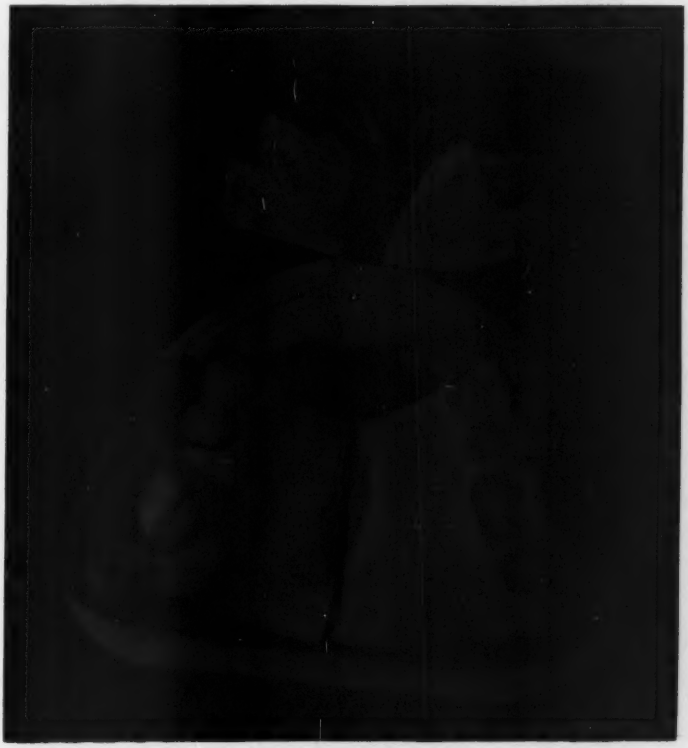

Figure 4.

Figure 5.

cut or scrape the model and the case will then be doomed to failure at its inception. When burnishing wax from the margins it may be found that some overextended feathered edges will result in the finished casting. This in no way alters the fit of the case for they can be readily removed before seating the bridge on the stone model or in the mouth.

After the wax three-quarter crowns have been completed, the pieces of model are assembled and fastened with sticky wax and the model, with its opposing member, is mounted on an articulator. The facings are then ground, placed in position, and a plaster-of-paris matrix that

covers the facings and the abutment teeth is constructed. Plastic or metal backings are selected, trimmed, and built up with wax to reproduce the lingual surfaces. The facings with the backings in position are returned to the plaster matrix and the matrix is carried to its position on the model. The waxed lingual surfaces are connected to each other and to the three-quarter crowns, the matrix is removed and adjustments to insure correct articulation are made. The case is sprued on the lingual aspect and after the contact points have been slightly exaggerated to permit polishing of the completed case without loss of contact, the facings are removed and the case is invested and cast (fig. 4).

As previously mentioned, the burnishings of the wax margins of the three-quarter crowns may result in slightly overextended feather edges. These should be slight and their removal will in no way affect the fit of the completed case. Greatly overextended margins or exaggerated contact points will interfere with seating of the bridge; however, the former must be avoided in the waxing process whereas the latter are readily removed in polishing. With the exception of the margins, polishing is completed in the laboratory. In the mouth, light polishing of the margins with fine disks is all that is required (fig. 5).

CONCLUSIONS

Construction of anterior bridges by means of one-piece castings is entirely feasible with the accurate impression materials that are available today. Attention to details and accuracy of each step in the process is essential in the construction of fixed bridges whatever technic is used. However, with the technic described, bridges that fit more accurately can be constructed. In addition, the reduction of the number of sittings required should make this method the more desirable.

Hemagglutination by Neurotropic Viruses

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THIS article presents an elaboration of and addition to the studies recently reported by Olitsky and Yager (*1*) on the hemagglutination reaction of certain neurotropic viruses. To the present time, the neurotropic viruses which are capable of agglutinating erythrocytes, characteristically inhibited by specific antiserum, have been reported to be Columbia SK, Columbia MM, (*1*) (*2*), GD VII (*3*), mengo-encephalomyelitis, and encephalomyocarditis viruses (*1*). Of these, all agglutinated sheep cells with the exception of GD VII virus which reacted only with human group O erythrocytes. The Lansing strain of poliomyelitis virus has also been found to agglutinate sheep cells (*4*) (*5*), a finding not confirmed by some observers (*1*) (*2*). While these studies were in progress, an article appeared which indicated that the virus of Japanese encephalitis agglutinated sheep cells (*5*). As the following discussion will show, extensive experiments with this virus and not only sheep cells but a wide variety of erythrocytes from other species yielded negative results. In an earlier article (*1*) of the present series, emphasis was placed on the care that should be taken to avoid nonspecific readings and several factors leading to false reactions were described. Another nonspecific factor will be described, in addition to the results of other hemagglutination tests with several neurotropic viruses and a number of species of erythrocytes.

The methods of performing hemagglutination and specific antiserum inhibition tests followed those already described (*1*). To recapitulate the more important details: Washed erythrocytes in final concentrations of 0.25 percent were suspended in buffered, 0.02 M phosphate saline solution, *p*H 7.6, and the mouse-brain virus or normal mouse-

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brain for control, fresh or frozen, was employed in 1:5 suspension in 0.1 percent bovine plasma albumin (*1*) (*6*) in buffered saline solution. Final virus dilutions began at 1:10 to 1:20 and by twofold increases reached to 1:10,240. Tests were conducted at 4° or 5° C., 23° C., or, at times, also 37° C. and were read at half-hour intervals up to 2 hours, sometimes overnight. Observations were made only by the Salk-pattern method. The viruses and the species of cells employed in the present investigation are listed in table 1.

The results of many repeated tests with a number of neurotropic viruses and a wide variety of erythrocytes failed to show characteristic hemagglutination which is specifically inhibited by antiserum and such as has been obtained previously with GD VII (*3*) and Columbia SK, Columbia MM, encephalomyocarditis, and mengo-encephalomyelitis viruses (*1*).

Now and then agglutination was noted in dilutions up to 1:80 of one or another virus, with quail, mole, agouti, woodchuck, sheep, human (group O), and guinea pig cells (table 1). Further study of these reactions revealed that they were nonspecific or "false positives," owing to fragility, instability, spontaneous agglutination of the cells or to the particulate nature of the mouse-brain suspension. In the latter case, normal mouse brain reacted to an equal degree with the infected mouse brain that was used as a virus suspension.

In view of the fact that it has been suspected that Japanese encephalitis virus agglutinated sheep cells (*5*), tests were made, not only with the Nakayama strain but with four others: three swine strains, V–4948, V–4949, and V–4950, and one equine, V–2900, all ultimately obtained from the 406th Medical Laboratory. Since it has been stated (*4*) that it is essential to prepare cells from freshly drawn blood for a proper test, such fresh erythrocytes were obtained from pools derived from two to four chickens. These tests failed to yield characteristic hemagglutination by the Japanese encephalitis virus with either chicken or freshly-drawn sheep cells. To elaborate the test with this virus, additional tests were made with cells suspended in phosphate buffered saline solution at *p*H 6.8, 7.2, 7.7, and 8.2, using both agouti and sheep erythrocytes, with the diluent of the test materials also at the same *p*H values. Here again no characteristic agglutination resulted.

Nonspecific agglutination by suspensions of mouse brain.—It has already been stressed that normal mouse brain (hence also virus suspensions) can agglutinate different species of erythrocytes and thus give rise to false reactions (*1*). For example, in the present study, Eastern equine encephalomyelitis virus, in dilutions up to 1:80, agglutinated sheep cells following centrifugation at 1,500 r. p. m. for 5

TABLE 1.[1]—*The viruses and the erythrocytes employed in hemagglutination*

Virus	Cells																												
	Quail	Duck	Pigeon	Gray squirrel	Cotton rat	Sheep	Calf	Monkey	Paca	Mole	Pheasant	Agouti	Woodchuck	Capybara	Alligator	Frog	Pig	Raccoon	Chipmunk	Prairie dog	Opossum	Vole	Chicken	Human (group O)	Guinea pig				
Japanese encephalitis [2] (5 strains)						(a)						(a)													(a)				
Eastern equine encephalomyelitis (strain 86)						(a)						(a)	(a)												(a)				
Russian Far East encephalitis												(a)																	
Western equine encephalomyelitis (Rockefeller Institute strain)										(a)		(a)																	
Venezuelan equine encephalomyelitis	(a)									(a)																			
MEF1 poliomyelitis	(a)																												
Lansing poliomyelitis						(a)																							
Coxsackie Type I						(a)																							
Coxsackie Type II						(a)																							

[1] For additional results of other experiments see reference (*1*).
[2] Nakayama strain generally used; additional strains used in chicken—erythrocyte tests (see text).
[3] Nonspecific agglutination; negative under controlled conditions.

minutes. After centrifugation at 2,500 r. p. m. for 20 minutes, the further clarified supernate failed to react. Similarly, only the partially clarified, not the clarified, supernate of Japanese encephalitis, Western equine encephalomyelitis, and Russian Far East encephalitis virus suspensions agglutinated agouti cells.

In the following test, outlined in table 2, one of a series with similar outcome, normal mouse brain was suspended in a manner similar to that employed for infected tissue and the resulting 20-percent suspension was tested in its uncentrifuged state and after centrifugation at 3,000 r. p. m. for 20 minutes. Of the latter centrifuged material the topmost, clearest part of the supernate was removed and used as "upper supernate" and the lower part of this layer just above the sediment, less clarified, was pipetted off and designated "lower supernate." Final dilutions from 1 : 10 to 1 : 1280 of all three materials were made and tested, just as is done in a viral hemagglutination of sheep cells. The results clearly point to the occurrence of nonspecific agglutination, correlated with the degree of clarification obtained by centrifugation of the suspension of a normal brain tissue.

TABLE 2.—*The correlation between particles of a suspension and the degree of nonspecific agglutination using normal mouse brain and sheep cells*

[Numbers show degree of agglutination, 4 representing a complete reaction]

Mouse brain 20 percent suspension	Hours kept at 5° C.	Reciprocal of final dilutions of virus								Saline control
		10	20	40	80	160	320	640	1,280	
Upper supernate	1	—	—	—	—	—	—	—	—	—
	2	—	—	—	—	—	—	—	—	—
Lower supernate	1	4	4	1	—	—	—	—	—	—
	2	4	2	±	—	—	—	—	—	—
Sediment	1	4	4	4	4	4	4	4	—	—
	2	4	4	4	4	4	4	1	—	—

DISCUSSION

The present investigations were undertaken with the view that there may still be found a practical test of hemagglutination for neurotropic, or encephalitis, viruses other than those (GD VII (*3*), Columbia SK, Columbia MM, encephalomyocarditis, and mengoencephalomyelitis viruses (*1*)) for which positive results have already been obtained. The outcome of the large number of experiments here reported, in which several viruses and erythrocytes deriving from a wide variety of species were used, would indicate that this prediction has not as yet been fulfilled. On the other hand, even though large numbers of samples have now been used, the technique of the tests was essentially unchanged. Consequently is it justifiable to assume that perhaps a change here and there in method might reveal the desired result. Again, even though a number of additional species of

erythrocytes have been tried in this study, many more remain to be examined. The view previously expressed (*1*) on the possibilities for bringing into the light other positive hemagglutinations is, therefore, still being held.

The results recently reported by others on the agglutination of sheep cells by Japanese encephalitis and by Lansing viruses could be shown to be brought about not by the virus, but by the mouse-brain tissue, as such, present in the virus suspension. Verlinde and de Baan (*5*) have also stated that uncentrifuged normal mouse brains, even greatly diluted, agglutinate sheep cells. Attention is drawn to the fact brought out here and supplemented by the experiments reported in an earlier article (*1*) that the technique of hemagglutination by neurotropic viruses as contained in mouse-brain suspensions should be carefully controlled with respect to its variables to avoid confusion with nonspecific, nonviral agglutinations. One of the variable factors that appears to be significant is the degree of clarification of the viral suspension, since the degree of nonspecific reaction has been shown to be apparently correlated with the relative intensity of clarification of such suspensions obtained by means of centrifugation.

CONCLUSIONS

Attempts to bring about characteristic hemagglutination with the viruses of Japanese encephalitis (5 strains), Eastern, Western, and Venezuelan equine encephalomyelitis and Russian Far East encephalitis, as well as MEF1 and Lansing strains of poliomyelitis virus and the Coxsackie virus, types 1 and 2 Albany (Dalldorf) and erythrocytes from 25 different species of animals failed. Additional studies indicate that normal mouse brain in suspension may give false positive agglutinations.

REFERENCES

1. OLITSKY, P. K., and YAGER, R. H.: Hemagglutination by Columbia SK, Columbia MM, mengo-encephalomyelitis and encephalomyocarditis viruses; experiments with other viruses. Proc. Soc. Exper. Biol. & Med. 71: 719–724, Aug. 1949.
2. HALLAUER, C.: Agglutination von Hammelerythrocyten durch Murine Poliomyelitis-virus Stämme. Fourth International Congress of Microbiology, Copenhagen, Denmark, July 20–26, 1947. p. 257.
3. LAHELLE, O., and HORSFALL, F. L., JR.: Hemagglutination with GDVII strain of mouse encephalomyelitis virus. Proc. Soc. Exper. Biol. & Med. 71: 713–718, Aug. 1949.
4. BREMER, A., and MUTSAARS, W.: Agglutination des Globules Rouges de Mouton par le Virus de la Poliomyélite (Souche Lansing). Compt. rend. Soc. de biol. 142: 1194–1196, Sept. 1948.

5. VERLINDE, J. D., and DE BAAN, P.: Sur l'Hémagglutination par des Virus Poliomyélitiques Murins et la Destruction Enzymatique des Récepteurs de Virus Poliomyélitique de la Cellule Réceptive. Ann. Inst. Pasteur 77: 632–641, Nov. 1949.

6. OLITSKY, P. K.; YAGER, R. H.; and MURPHY, L. C.: Preservation of neurotropic viruses. U. S. Armed Forces Medical Journal 1: 415–417, Apr. 1950.

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Laceration of the Vaginal Vault After Normal Coitus

Report of a Case

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CHARLES H .GILLILAND, *Commander (MC) U. S. N.*[1]

VAGINAL injury as a result of normal coitus has always been considered a rarity and only brief references are made to it in the standard textbooks. The general impression is that this type of injury occurs only in virginal and postmenopausal woman and is usually the result of violent rape or an abnormal sex act. Diddle,[2] however, in reviewing the literature, found that in the past 76 years, 133 cases of major tears of the vaginal vault resulting from coitus were recorded. The majority of these persons were in active menstrual life. Diddle's review also emphasizes the fact that this accident is more common than is usually realized, as many cases must go unreported and many more must go unrecognized. Moreover, this injury may be very serious. The following case is reported to emphasize further these facts and to add another case report to the literature.

CASE REPORT

E. R., a 22-year-old white primigravida, was delivered of a full-term viable infant at the U. S. Naval Hospital, Bethesda, Md., on 13 February 1949.

Except for a few clots noted in her lochia on the fourth postpartum day, her course was entirely normal. A right mediolateral episiotomy healed without incident. She left the hospital on the sixth postpartum day.

In the 5 weeks between the delivery and the first coitus, she was well. Following the first coition after delivery, however, she noted some bright red spotting. This occurred following each act until 29 May 1949, 15 weeks after delivery, after which date she had three successive copulations without any bleeding. On 0100, 5 June, 16 weeks after delivery, following intercourse she passed a large clot of blood from the vagina and her local physician advised her to report to this hospital.

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[1] U. S. Naval Hospital, National Naval Medical Center, Bethesda, Md.
[2] Diddle, A. W.: West. J. Surg. 56: 414, July 1948.

On physical examination a moderate degree of lower abdominal pain was noted. The temperature was 99.4° F.; pulse, 96; blood pressure, 90/60; general physical examination was essentially normal. Upon inserting a speculum into the vagina, about 450 cc. of liquid and clotted blood poured from the vagina. A tear, 3 cm. long, was seen in the right anterior vaginal vault at about 10 o'clock. A steady flow of bright red blood was coming from this rent that seemed to involve the entire thickness of the vaginal wall. The episiotomy scar was well healed.

Oxycel was placed over the laceration and a vaginal pack was inserted to hold it in place. The pack was removed in 24 hours. Bleeding started again, about 24 hours later, and another pack was inserted but the hemorrhage continued. The patient was taken to the operating room and the defect closed with No. 00 chromic sutures. Penicillin, 100,000 units every 3 hours, was administered. She was discharged in good condition the next day. An examination, 2 months later, revealed good healing of the wound.

The Clinical Use of Antibiotics

I. Pharmacology and Toxicology [1]

PERRIN H. LONG, *Colonel, MC, A. U. S.*[2]

THE development of the sulfonamides and antibiotics in the past 16 years has had especial significance in the field of military medicine. Although great progress in sanitation and certain prophylactic procedures in the Armed Forces had been made since the Spanish-American War, nevertheless in World War I and in subsequent years, prior to the advent of the sulfonamides and antibiotics, deaths from infectious diseases took their toll in the Army, Navy, and Air Force. It is true that mortality rates from certain infectious diseases in the Armed Forces had been constantly falling for almost 50 years, but every older medical officer can remember his helplessness as a process of infection pursued its natural course. All can remember the fear created by the appearance of scarlet fever, meningococcal meningitis, and a number of other infectious diseases on the post.

With the development of the sulfonamides in the late 1930's, medical and dental officers no longer had to stand by helplessly and watch a patient with meningococcal meningitis develop a serious complication or perhaps die, or see an initially mild gingival infection develop into a Ludwig's angina. Armed with active chemotherapeutic agents they could arrest and cure what formerly were highly fatal diseases. As new sulfonamides were developed and as penicillin, then streptomycin, bacitracin, aureomycin, and chloramphenicol were introduced, the ability of the officer to cope with infectious processes was greatly increased. The use of penicillin in the Armed Forces from 1943 on was an important factor in the extraordinarily low mortality rate noted in the Armed Forces during World War II. The prompt and widespread use of antibiotics in treating infectious diseases also acts

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[1] This is the first of four articles on this subject. The second will appear in the September issue.

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as a control measure in their spread by reducing the period of contagion. At present, with the exception of a few viral diseases and bacterial infections produced by *Pseudomonas aeruginosa* and *Proteus vulgaris*, medical and dental officers have at their disposal potent agents with which to combat infectious processes.

In this multiplicity of anti-infective agents, and especially in the use of these antibiotics, there lies a pitfall. With so many sulfonamides and antibiotics available for the treatment of a given infectious process, with the supposed merits of each therapeutic agent being extolled in medical and dental reports, and with the announcement of new antibiotics appearing almost monthly, it is difficult for medical and dental officers to decide which is the best and proper antibiotic to use. This series of articles will point out the current thoughts concerning the selection and the use of antibiotics for the treatment of infectious diseases.

PHARMACOLOGY

The medical or dental officer who employs antibiotics cannot do so rationally without an understanding of the clinical pharmacology and toxicology of these agents.

Tyrothricin is effective against gram-positive organisms. It must only be used as a topical agent, and under this condition little is absorbed. It cannot be used for the systemic treatment of infections because it produces a severe hemolytic anemia. As it is chemically a polypeptide it does not sensitize the skin, although in ointment bases or in alcoholic solutions preparations of this agent may irritate the skin of certain patients.

Bacitracin is effective against gram-positive and certain gram-negative micro-organisms. It is used only as a topical agent or for the limited local infiltration of certain infectious processes, because when it is administered parenterally for its systemic effect it may produce renal damage. It is not stable. Solutions of bacitracin should be kept in the ice box and not used after they have stood for 3 weeks.

Penicillin may be used by the oral, topical, or parenteral route. As a great portion of the antibiotic is either destroyed or not absorbed when it is administered orally, it is necessary to give about five times as much penicillin by mouth per dose than is necessary when crystalline penicillin G is being administered in aqueous solution parenterally. Crystalline penicillin G, when given intramuscularly in watery solution, is rapidly absorbed and after a few hours is not detectable in the blood stream. Procaine penicillin G, in watery suspension, in oil, or in oil with 2 percent aluminum monostearate added, is absorbed with varying degrees of slowness following its intramuscular injection.

Detectable concentrations of penicillin in the blood can be found for from 12 to 24 hours after a single injection of 300,000 units of procaine penicillin G in an aqueous suspension, for about 48 hours after the injection of a like amount of procaine penicillin G suspended in a vegetable oil, and for about 72 hours following the injection of a similar amount of procaine penicillin G suspended in a vegetable oil to which 2 percent aluminum monostearate had been added.

Penicillin, when absorbed into the blood stream, is rapidly excreted in the urine. It does not diffuse readily into brain, nerve, bone, and other tissues, and in normal persons the diffusion of penicillin into the cerebrospinal fluid is slow and inconsistent. It passes slowly into synovial, pleural, and pericardial fluids, but interestingly enough, it diffuses readily into ascitic fluids. It passes easily from maternal to fetal blood, but not readily to the vitreous or aqueous humors, milk, sweat, tears, or saliva. It does not diffuse readily into abscess cavities. Its excretion by the kidneys can be slowed or blocked by the administration of certain compounds which inhibit the renal tubular excretion of penicillin. When such compounds are used, higher plasma concentrations of the drug may be obtained than are otherwise noted from similar dosage. From a practical point of view, benemide is the most satisfactory agent to use for this purpose at present.

Streptomycin and dihydrostreptomycin behave similarly in the body. When they are administered by mouth in therapeutic doses, absorption is practically nil and they cannot be easily detected in the blood or urine. The same is true when streptomycin aerosols are inhaled. Following intramuscular injections of streptomycin, peak levels of the drug in the blood are noted within 1 to 2 hours and only small amounts of it are found in the blood 4 hours after the injection. In the tissues, streptomycin is distributed solely in the extracellular water. It passes over very slowly into cerebrospinal, synovial, pleural, and pericardial fluids, and, when found in these fluids, is always present in a much lower concentration than that found in the blood. It diffuses readily into peritoneal fluid and into the aqueous and vitreous humor. In the fetal blood, concentrations of about one-half of those in the maternal blood have been noted. Following a single intramuscular injection of streptomycin its excretion is greatest by the kidneys within 2 hours, and within 24 hours the bulk of the drug will be excreted in the urine. A little is excreted in the bile. When renal function is impaired the rate of excretion of streptomycin is decreased, and the drug accumulates in the blood.

Aureomycin.—When this drug is administered by mouth in a single moderate dose, maximal absorption, as measured by its concentration in the blood serum, appears to take place in from 2 to 6 hours, and detectable quantities of the antibiotic may be present in the

blood stream for at least 12 hours. The drug has been noted in emulsions of the liver, kidney, spleen, and lungs of patients who died while receiving aureomycin, but nothing is known as to whether it diffuses into the intracellular water of the cells of these tissues. It is suspected that it does, and certainly it must penetrate the endothelial cells. Otherwise it would be difficult to explain the action of aureomycin on *Rickettsia*. This agent does not easily pass the blood brain barrier in human beings, but, when infection of the meninges is present, it is possible to detect it in the cerebrospinal fluid. It passes into the bile and milk in fair concentrations. As yet it is not known whether it diffuses into the vitreous or aqueous humor. From 12 to 15 percent of a single dose of aureomycin can be recovered from the urine, in which it may be excreted for as long as 72 hours following a single dose. In the urine, concentrations of several hundred micrograms of the drug are easily obtainable following moderate and repeated doses. It passes the placental barrier, and appreciable amounts can be detected in the cord blood of the infant if the mother is receiving aureomycin. With multiple doses of aureomycin, given every 6 hours, concentrations of 2.5 to 20 micrograms of the drug have been noted in the blood stream.

It appears that following an intravenous dose of aureomycin, maximal concentrations of the drug in the blood are reached within 5 minutes, while detectable amounts may be noted for as long as 12 hours. Also it has been observed that relatively small amounts of aureomycin, injected intravenously, will produce excellent concentrations of the drug in the blood of the patient. This observation is of importance to the physician when he is considering the use of aureomycin in critically ill patients. Much is unknown about its pharmacology, and a further delineation in this field awaits the determination of the chemical structure of aureomycin. Aureomycin is, however, quite well absorbed when given by mouth; is probably distributed in both the extra- and intra-cellular tissues of the body; is excreted mainly in the urine; and the majority of aureomycin, as such, is destroyed in the body. There is no evidence that renal dysfunction lessens the excretion of aureomycin in the urine.

Chloramphenicol is a crystalline substance; chemically it is a nitrobenzene compound. It can be synthesized. It is relatively insoluble and for that reason the oral route of administration is preferred. When a single moderate dose is given by mouth, maximal concentration of the drug in the blood occurs within 2 hours and then declines, and at 8 hours detectable amounts of the agent are not present in the blood. While extensive studies have not been made, it would appear that chloramphenicol is well distributed in the body tissues. It un-

doubtedly is present in both the intracellular and extracellular body water. Otherwise it would not be so effective in the control of rickettsial infections. It passes over readily into the cerebrospinal and pleural fluids and is found in appreciable quantities in the bile. The placenta offers no barrier to its passage and the concentration of chloramphenicol in cord blood is about 75 percent of that in the maternal blood within 2 hours after the administration of a single dose. Chloramphenicol is excreted mainly in the urine, in which it appears in appreciable quantities within 30 minutes after the administration of a single dose. When multiple doses are given, little difficulty is encountered in maintaining high concentrations of the drug in both the blood and the urine. It is not yet known whether it passes into the vitreous or aqueous humors.

Both chemical and biologic tests are available for the detection of chloramphenicol and its break-down products in body fluids and tissues. A comparison of the two tests, on like samples of blood from patients who are receiving chloramphenicol, shows that for the first few hours after the drug has been administered both tests give comparable readings. Then, however, the chemical values mount, while the biologic values drop, indicating the conversion of chloramphenicol to an inactive form in the body. In the urine this difference is always great and the chemical test gives readings about 10 times greater than those of the biologic test, again indicating that the majority of chloramphenicol that has been excreted is in an inactive form. There is no evidence that renal dysfunction impairs the excretion of chloramphenicol in the urine.

TOXICOLOGY

Tyrothricin, as prepared for topical use, does not produce toxic reactions, although preparations of tyrothricin may irritate the skin of certain patients.

Bacitracin, as prepared for topical use, rarely produces toxic reactions. Dermatitis appears in about 0.5 percent of patients who are treated with topical applications of this agent. There is, however, the possibility that when bacitracin is used as a local infiltrating agent in certain infectious processes, enough will be absorbed systemically to produce renal injury. The renal injury that has been described when this drug has been used experimentally, for the systemic treatment of infections, is tubular in nature and varies in intensity with different lots of bacitracin and with the susceptibility of different patients to this type of tissue damage.

Penicillin.—The main toxic reactions resulting from the administration of penicillin are those of sensitivity to the drug or to its products. They consist of drug fever, various types of skin lesions, asthma,

anaphylactic phenomena, or a combination of these signs and the symptoms thereto attendant. Previous fungal infections may sensitize a person to penicillin. Certainly, repeated courses of therapy increase the possibility of an allergic state being produced, and without doubt the topical use of penicillin on certain mucous membranes, and especially on abraded or weeping surfaces, is likely to produce sensitivity to the drug. The inhalation of penicillin or its topical use in the oropharynx often produces direct irritative effects on the tongue (black tongue) and mucous membranes of the nose and throat, and at times asthmatic states are induced in this way. Reactions of sensitivity may occur within a few minutes after the administration of penicillin, or they may not make their appearance until days, weeks, or even months after treatment with the antibiotic has been discontinued. These episodes of toxicity may be multiple or single. Among the reactions noted in the mucous membranes or skin are stomatitis and glossitis, glossodynia, black tongue, and varicelliform, morbilliform, bullous, or purpuric eruptions, urticaria or angioneurotic edema with or without pruritus, pruritus without rash, exfoliative dermatitis, dermatophytosis, activation of old dermatophytic foci, the "id" reaction, and in rare instances severe keratitis with sloughing of the cornea. Neurologic disturbances resulting from the relative or direct toxic effect of penicillin have been noted. Crystalline penicillin applied directly to the central nervous system has an irritative effect. Peripheral neuritis, involving various nerve trunks, has been described but is uncommon. Penicillin is not an innocuous substance, and severe toxic reactions and even death have followed its use.

Streptomycin and dihydrostreptomycin.—The most common toxic reactions noted in the course of therapy with streptomycin are those resulting from the development of sensitivity to the drug. These reactions may take the form of a drug fever, of varying types of dermatitis, or they may resemble serum sickness. In some patients the dermatitis may be exceedingly severe, taking the form of a dermatitis exfoliativa. It would appear that streptomycin is more prone to produce sensitization of the skin than any other of the antibiotic drugs and, because of this, persons who come frequently in contact with streptomycin (nurses, physicians, pharmacists) should protect themselves by wearing gloves, masks, et cetera, when handling this drug. Another toxic reaction which may occur is vertigo or deafness or a combination of both. The vertigo is apparently produced by a toxic effect of the drug on the vestibular apparatus. There appears to be a direct relation between the occurrence of vertigo and the amount and period of time in which the agent is given. Since smaller doses of streptomycin have been used in the treatment of certain diseases (notably tuberculosis) the incidence of this toxic reaction has greatly decreased.

If vertigo makes its appearance and is mild, therapy may be continued. If, however, the degree of vertigo is progressive, the drug should be stopped. It would seem best always to stop it if deafness becomes apparent. Among the other toxic reactions which have been noted are eosinophilia, evidence of renal irritation when the urine is acid, and nausea and vomiting. These are unimportant or easily controlled so they are not indications for stopping treatment. There would appear to be little clinical difference in the over-all toxicity of streptomycin and dihydrostreptomycin.

Aureomycin.—To date, aureomycin has not produced more serious toxic results than nausea and vomiting, and questionably a mild dermatitis. The nausea and vomiting produced by aureomycin are apparently becoming less common as this drug is produced in a purer form. Patients who receive therapeutic doses of aureomycin frequently have several loose stools a day during the period of treatment. This probably is the result of a disturbance in the bacterial flora of the colon produced by aureomycin. Sore mouth may occur from the use of aureomycin in the form of troches or when the drug is used as a mouth wash.

Chloramphenicol.—Toxic reactions occurring in the course of therapy with this drug are uncommon. Nausea, vomiting, drug fever, and mild skin eruptions have been noted. Granulocytopenia associated with an arrest in maturation of the various elements in the bone marrow has been observed. For this reason, total white blood cell and differential counts should be made at frequent intervals in patients who are receiving chloramphenicol. Frequent loose stools may occur.

SUMMARY

Effective antibiotics are now available for the treatment of most bacterial, all rickettsial, and certain viral infections. A knowledge of the clinical pharmacology of these agents is a prerequisite for their use. The clinical toxicologic properties of antibiotics are many and varied and must be thoroughly understood by medical and dental officers, in order that their patients may receive maximal protection from the harmful effects of these extremely important therapeutic agents.

Acute Abdominal Manifestations of Ancylostomiasis

Report of Two Cases

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HOOKWORM has been little considered in texts dealing with acute abdominal syndromes. Recently reference has been made to hookworm simulating duodenal ulcer (*1*) (*2*) and mimicking surgical conditions of the abdomen (*3*). In the Tropics hookworm is commonly encountered, and is frequently associated with acute abdominal syndromes. In 1948, 224 patients were admitted to this hospital with a primary or secondary diagnosis of intestinal ancylostomiasis. Of these, 21 were admitted to the surgical service complaining of abdominal distress of sufficient severity to warrant a tentative diagnosis of an acute abdominal inflammation. Among the patients admitted to the medical service there were 10 of a similar nature.

The average age of these 31 patients was 29 years: 28 were male and 3 were female native Panamanians. The admitting diagnoses are shown in table 1, and the location of the pain is shown in table 2. In most patients the pain was cramping and well localized. The onset was usually gradual over a period of a few days. The pain varied in intensity from mild cramps to excruciating spasms. Associated tenderness was present in 25 and in 2 boardlike rigidity was observed. The pain was accompanied by nausea in 20 patients and by vomiting in 9. In one patient the vomiting was so severe that high intestinal obstruction was suspected. Diarrhea was observed in only two patients. Constipation was not noted. Rectal tenderness, psoas spasm, and shock were not encountered. Thirteen patients had a temperature of 99° F. or over. The highest was 104° F. An elevation of the white blood cell count over 9,000 was observed in 13 patients, 3 of whom had a polymorphonuclear cell count of over 80 percent. Eighteen patients had an eosinophil count of over 4 percent; the highest was 27 percent. These patients entered the hospital from 3 hours

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to 4 months (average 3 days) after the onset of symptoms. The pain was in no way related to the taking of food.

TABLE 1.—*Admitting diagnosis of 31 patients with ancylostomiasis*

Appendicitis	10	Dysentery	1
Original correct diagnosis (ancylostomiasis)	10	Intestinal obstruction	1
Gastro-enteritis	2	Tumor of sigmoid	1
Peptic ulcer	2	Perforated peptic ulcer	1
Food poisoning	1	Cholecystitis	1
		No abdominal pain	1

TABLE 2.—*Location of pain in 30 patients with ancylostomiasis*

Epigastrium	9	Left lower abdominal quadrant	4
Right lower abdominal quadrant	8	Periumbilical	2
Right upper abdominal quadrant	6	Generalized	1

CASE REPORTS

Case 1.—A 47-year-old laborer was admitted at 1500 complaining of a severe epigastric pain that came on suddenly after drinking a glass of water 4½ hours earlier. The pain was lancinating, localized, and accompanied by nausea. He had had periodic attacks of a similar but milder pain in the past several years. His conjunctivas and mucous membranes were pale. There was tenderness and cramping in the epigastrium and right upper abdominal quadrant. His temperature was 101.4° F; pulse rate, 100; and respiratory rate 22. The erythrocyte count was 3,610,000 with 70 percent hemoglobin. The leukocyte count was 10,200 with 2 percent eosinophils. A Levin tube was placed in the stomach and attached to a suction apparatus. The patient was given intravenous fluids. Serum amylase was 36. Within 8 hours all symptoms and signs had disappeared completely and the temperature was normal. Hookworms were found in the stools and were eliminated by appropriate treatment.

Case 2.—A 33-year-old chauffeur was admitted with a history of gradually increasing cramping pain of 1 week's duration in the right lower abdominal quadrant and right flank. In the past 2 years he had had two attacks of a similar, but less severe pain. Although the present attack was unaccompanied by nausea or vomiting, the patient noted that his stools were softer than normal. A mild burning on urination had been noted several times in the immediate past. On physical examination, superficial and deep tenderness in the midabdominal region was noted. Slight tenderness was present in the right costovertebral angle. The erythrocyte count was 3,762,000 with 75 percent hemoglobin; leukocyte count was normal, but repeated differential counts showed 5 or 6 percent eosinophils. Two successive stool examinations disclosed hookworms. The patient was treated and discharged cured.

COMMENT

These patients have presented a difficult problem in diagnosis; we have to recognize them largely by the varied clinical findings. The symptoms and signs do not follow the general pattern of events seen in acute conditions within the abdomen. Most of these patients have been undernourished and have shown evidence of anemia. We

treat them expectantly and observe them closely. The signs and symptoms usually improve promptly and stool examination confirms a diagnosis of hookworm. We have been aided by a staff of trained technicians who give us prompt and accurate reports of stool examinations. In this group of patients, none of whom were operated on, close observation and study prevented needless operations.

References

1. Monat, H. A., and Cooper, I. S.: Duodenal ulcer and hookworm infestation; diagnostic and military medico-legal problem. U. S. Nav. M. Bull. **47**: 338–342, March–April 1947.
2. Yenikomshian, H. A., and Shehadi, W. H.: Duodenal ulcer syndrome caused by ankylostomiasis; report of 25 cases with gastric acidity and roentgenological studies. Am. J. Roentgenol. **49**: 39–48, Jan. 1943.
3. McEwan, D.; Economon, J. G.; and Zellner, R. E.: Mistaken surgical diagnoses in hookworm disease. South. Surgeon **13**: 760–766, Oct. 1947.

The Transition of the Citizen Into the Wartime Armed Forces

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NEVER is it more important to understand the particular prevailing national circumstances than when enlisting Armed Forces personnel. No matter how effectual a plan in terms of peacetime practice designed to fit a particular situation may be, that plan is likely to be entirely unsuitable when applied under the circumstances of war. Further, the methods employed in one war are likely to be inefficient in another, and no two countries could use an identical system with equal success.

Many military men insist that, given the men, they will make the soldiers. What these officers really believe their mission to be is to train a man forcibly into a specified type regardless of the capabilities or natural bent of that man. All those who fail to measure up or those who break down mentally or physically are considered to have been impossible material from the beginning or fit only for fatigue duty. Their solution is very simple: Take your pick of the end product, return the others, complain about the men supplied, and let someone else worry.

There is some justification for this method under a voluntary system or during a limited war where the manpower needs are not great. If better means of selection would not be advantageous under the conditions it could be expedient to accept a trial and error method.

However, during a state of total war when demands on human effort exceed the available supply for the national effort as a whole, it will be necessary to increase the efficiency not only in the proper selection for service or civilian occupation but to make sure that "make or break" methods in training and employment do not waste manpower, time, and money.

It would seem relatively simple to devise an efficient system of selection, induction, and job placement and training were it not for two

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factors: (*a*) the inscrutable nature of the human personality and (*b*) the enormous difficulty in accurately predicting individual capabilities under wartime conditions. There is a great need for further research in the evaluation of these factors of human behavior. In spite of great advances in psychiatry and psychology we still cannot forecast the course of human behavior. Everyone accepts the thesis that it is sensible to place round pegs in round holes but many regard this as a matter that can easily be solved by a few simple tests rather than as a difficult integration of job fitness with job requirement. Until we reach a stage of thought control and subjugation of man's emotions, there will always be great difficulty in compelling persons to do what they do not want to do, or in restraining their liberty by force. The very restraints imposed in the Armed Forces are likely to make individuals react differently than they would in a natural peaceful environment.

However, this does not mean that psychiatric and psychological studies are not effective; in fact, the reverse is true. It means that well-trained psychiatrists and psychologists working in teams must have time and facilities to carry out their studies on the individual. It is not only the problem of screening out totally unfit persons but also the more important problem of carefully estimating the personality, skills, aptitudes, and motivations of recruits and recommending appropriate placement. There are great masses of persons with personality defects of all sorts; few persons do not have some deviation from the ideal. But, if they are intelligently placed, the majority can be suitably employed somewhere in the Armed Forces. The normal is, after all, the average of the civil population and the Armed Forces cannot possess numbers and quality that do not exist. Neither should the Armed Forces forget that they are in essence that segment of the Nation's population who, backed by the will and support of the rest of the Nation, actually carry out the policy of war by force of arms. They are then of the people and are responsible not only for the successful operation of the war but also for the proper employment and care of those entrusted to them. When peace is restored these citizens in the ranks return to civil life to take their place in the national effort of reconstruction and in the life of the democracy.

Even with his defects, man is very adaptable. For the love of God and his country, for lofty ideals, for survival, for love of his fellowman, or for many lesser motivations, he can transcend his mundane existence and rise to great heights of heroism or sacrifice. He is motivated to freely accept the conditions of the Armed Forces and give of his best to the extent that he is activated by these devotions and willing, even anxious, to play a part in his country's need.

Many, whose motives are purely selfish, or at least show little evidence of higher ideals, will accept service willingly enough merely because of their liking for certain phases of it. Some accept it as a means of escape from an unsatisfactory environment. Others accept it because there is no other way out.

The incentive to serve well can be killed even in men with the finest motivations, through bad handling and disillusioning experiences. At all stages in the soldier's career the desire to serve must be fostered. It is stupid to promote enthusiasm by sentimental exhortation and promises and then kill it in the early days of service. First impressions of service life are apt to be the most lasting. Introduction to hard training should be gradual rather than a sudden application of discipline that is so often practiced. Never is intelligent leadership more significant than in the early stages of training. Once a man can see the reasons for regulations and has the feeling that he is being fairly dealt with, he usually adapts himself quickly to the needs of the group. Thereafter, if he can realize that the inherent strength of the group is greater than his own he is well on the way to becoming a good soldier. If, however, he conceives that he is an outcast or misfit, unfairly disciplined, or so badly treated that he becomes resentful, or is made to obey through fear alone, then his future usefulness to the Armed Forces will not be hard to predict. Unless he is "mentally rescued" by an improvement in man management or individual psychiatric attention he soon will become motivated to escape rather than to serve. In time, unless conditions are corrected, or even in spite of correction, he will, in all likelihood, either attempt to "work his ticket" out of the service through some form of dissimulation, become a chronic offender, or show neurotic behavior or evidence of a psychosomatic disorder.

Of course, mental or psychic breakdown can occur at any stage of training or operations, but it is believed that the most critical period is during the early stages of adjustment to the service. Emotional conflicts set up and not resolved at this stage, probably account for many of the disturbances that appear later when exposed to additional stress. There are those who still believe that early selection should eliminate all those with any neurotic behavior patterns (if it were really practicable to do so) and thenceforth they assume that neurosis will not occur. Certainly the experiences of the last war do not seem to bear out their contentions. Unselected men appeared to show no higher breakdown rate than those who were selected. Unfortunately there is no means of now knowing how well those who were turned down at examination would have done had they been accepted.

If we can then assume that the early period of transition from civil life to service environment is as important to the production of good

soldiers as is believed, let us consider some general principles in the machinery of selection and period of induction which would favorably or unfavorably influence success.

Let us begin with the individual, rather than the State or the requirements of the Armed Forces. In a free democracy, as opposed to a tyranny, the government or State exists through the collective will of all citizens supporting their freely nominated representatives by secret ballot. The necessity for voting at agreed intervals so that representatives may be tested as to their views or record against those of a contrary opinion is inherent in the system. The pros and cons of policy are freely debated before the people. It is theirs to choose. To avoid a chaotic multiplicity of group views, those of similar views usually group themselves into as few parties as possible. Since strength must be met by strength, there is a natural tendency to form into two main groups. But in the nature of things there must be not less than two groups if democracy is to survive. One-party rule inevitably leads to tyranny and the abolition of the ballot.

The free democratic citizen then is conditioned to freedom of expression. Indirectly, but surely, he influences his country's foreign affairs and through his individual ballot influences war or peace. If, before war he is opposed to war at any price, it will take a great deal of persuasion to overcome his distaste if war occurs. In the final analysis, he, as a free citizen, has the right to his opinion one way or another. He is conditioned to fighting out the pros and cons of his viewpoint at the polls and accepting the majority verdict with more or less good grace. Unless he can understand that war was inevitable or necessary and not the result of mismanagement by the people's representatives, his aversion to war is understandable.

In a cross section of the population there are all shades of viewpoint and all varieties of individual circumstances and social and financial pressures varying with the times. If a man is of military age and total manpower mobilization is necessary he is faced with suddenly relinquishing his freedom and being told either to work at a specific occupation or be inducted into the services. The entire pattern of his life may be changed overnight. The farmer, the office worker, the merchant, or student, whether self-employed or independent, must give up what he is doing and enter into a strange environment. He is usually beset by many difficulties incidental to winding up his affairs, or making special provisions for his family. No matter how willingly he sets out, it is a period of great emotional stress and uncertainty. He has heard many tales of glory and of death. He wonders what the fates have in store for him and invariably hopes for the best. He is in a very receptive mood for a guiding hand and a

sympathetic mentor. Under the protective coloration of the bravado of youth lie his mixed emotions, motivations, and hopes waiting to be guided harmoniously into the ways of a new life, the paths of which seem so uncertain.

Is it any wonder that the sensitive young man who finds himself suddenly reduced to a number, subjected to bullying remarks and commands, and thrown among strange incompatible bedfellows suffers intensely and begins to brood on escape? The transition often is a greater shock to his psyche than his seeming indifference would indicate. In the democratic way of life it is not taught that all men shall regard all others as congenial or that all orders or whims shall have the sanctity of the law. The Armed Forces might also recall that their organization is not a business. It is patterned on an early aristocratic tradition of autocratic rule which the passage of time and social change has modified but neither erased, nor always improved. Within their jurisdiction they can still show either the benevolent or tyrannical aspects of their character. This essential difference in the way of life in the Armed Forces to that in free democratic civil life is basic to an understanding of the great social and emotional adjustment that the recruit must make. Long ago there was less difference between the two ways. There is less difference today in many countries. A question at issue might be "Are we to have more democracy in the Armed Forces or less democracy in civil life?". The latter alternative has been the invariable solution of dictators of whatever stripe, for only in this way can they control both the people and the Armed Forces.

Now we must consider where the medical examination and selection of personnel takes place and how they are allocated for particular duties.

If we presume conditions of total war and some form of compulsory allocation according to apparent requirements, then it is obvious that long and detailed studies of manpower resources must be carried out well in advance and kept up to date. The relative requirements in industry, farming, essential services, and so forth, and the Armed Forces then can be arrived at roughly and a balance struck.

But there is one great unknown factor. Who and how many are mentally and physically fit for service, and if fit with or without limitation, how can these persons best be utilized on the basis of their ability and motivation applied to specific service tasks?

The call-up cannot be faster than the capacity of the Armed Forces to assimilate personnel. Then in what order is it intended to draft them? Obviously if all the 18-year-olds were absorbed first the services could not expect to find tradesmen, technicians, or professional people. To

be really orderly in method, an exact distribution of required types would have to be known.

Are they to be medically examined in their home town or at an induction center or at both? If examined at the induction center, how much time shall be allotted prior to attestation? This last is of vital importance for several reasons: (*a*) too hasty examinations lead to errors; (*b*) there must be time for the proper study of the man's motivations and personality before reasonable selection can be made; (*c*) if there be too great an interval before attestation, the rejectee may find that his civilian job has been filled, thus creating unnecessary hardship (possibly preliminary screening is one way to resolve this difficulty); and (*d*) if there is no provision in special cases for the man to return to his home for a period following acceptance, how will it be possible to avoid hardship on the small businessman for instance who sells out on the expectation of acceptance only to find that he is unfit and has nothing to which to return? The service has a responsibility here.

Voluntary enlistment rather than compulsion avoids many of the above difficulties. A man could then ask for a medical examination and if fit return home to put his house in order before actually enlisting. His motivation toward serving is, in all probability, good. There is less likelihood of early mental conflict if he has the feeling of free choice.

Yet, if after enlistment he finds that he is allocated against his will to a branch of the service which he dislikes or considers unsuited to him, he is apt to feel that his free will is unnecessarily restrained and may, in consequence, react much like those who are drafted.

Would it not be wise under a compulsory system to offer, as a compromise, as much free choice at various stages as is possible? Could not examination for all three services take place at one center and, after a reasonable interval during common basic indoctrination and training, the selectee be given freedom of choice of service? Later could he not be given a reasonable latitude of choice as to particular branch? (Subject, of course, to special fitness or aptitudes that may be required.) Surely this humanization of policy rather than blind worship of establishment tables would be feasible and there is no doubt that it would reap great dividends in human efficiency.

The placing of induction and early training centers is of importance. It is most desirable, during the early period of transition from civil to service life, that the man be kept as near home as possible. The other men also come from his area and they have much in common. He has both male and female friends and relatives nearby. It is much easier for him first to learn the strength of group association and the

need for discipline and self-control among those whom he understands than among complete strangers. There is plenty of time for wider and wider associations. Haste should be made slowly. Administrative and training plans disregarding this important concept will surely cause futile manpower wastage.

Above all, the initial examination, indoctrination, and common basic training centers set up must be most carefully staffed. This is a key position which demands officers and noncommissioned officers who possess a knowledge of human relations and are favorably known and respected throughout the area for good character, integrity, justice, and inborn leadership. There is no place here for martinets who know no other means of leadership than that of command through fear. There are unfortunately too many of them to be met later in the soldier's, sailor's, or airman's career, when it is hoped he has acquired a safer mental adjustment, or that the overt disciplinarian has been curbed through an enlightened policy. At the initial training center, the individual should begin to feel his common identity as a citizen and a soldier and that as a citizen he is not being set apart from others, but is to serve so as to most suitably express his free political will in opposition to the enemy. Having achieved that concept, his objectives become clearer. He can then settle down to pursue his mission in the war with resolution, knowing that the sooner it is successfully concluded, the sooner he can again employ his knowledge, experience, and new and old skills in the peaceful reconstruction which must follow.

The Armed Forces, however, can only proceed so far in their efforts to successfully utilize manpower. Unless the national morale has been so molded by national leadership both before and during war so that the masses of the people have pride and faith in their Armed Forces and the common cause, and wholeheartedly support them, the Armed forces cannot hope to achieve final success. In other words, the degree of faith and belief in the righteousness of the cause which is inherent in the national motivation and morale will directly determine the real effectiveness of the Armed Forces.

About The Army Medical Department

Medical Department Extension Courses [1]

HOWARD S. MCCONKIE, *Colonel, MC, U. S. A.*[2]

EXTENSION courses of one or more of our Army schools are converted to correspondence courses. They were first used in the Armed Forces in March 1907 by the National Guard of the State of Indiana which at that time instituted a correspondence course in military medicine for its medical officers. In 1910, the War Department authorized a correspondence course for its medical officers, and in the following year the Army Field Service and Correspondence School for Medical Officers was organized as one of the Army Service Schools at Fort Leavenworth, Kans. This was authorized for members of the Regular Army Medical Corps only. The majority of our extension-course students today are Medical Service Corps officers and enlisted men desiring Reserve commissions in that Corps.

The Medical Reserve Corps of the Army was created in 1908. It was the first integral volunteer reserve ever organized in the Army. In 1915, a correspondence course was authorized for the several corps of the Medical Department Reserve. These were discontinued during World War I. They were reinaugurated at the Medical Field Service School at Carlisle Barracks, Pa., when the War Department established the army-wide correspondence system in 1922. That system remained in effect until the mobilization for World War II. Courses were prepared by the Medical Field Service School and were administered by the nine corps areas then in existence. Those subcourses [3] were normally graded by the Regular Army Medical Department personnel located nearest the student. Possibly such a grader was on

[1] Presented at First Army Medico-military Symposium, Governor's Island, 26 April 1950.

[2] Chief, Extension Courses Department, Medical Field Service School, Brooke Army Medical Center, Fort Sam Houston, Tex.

[3] Correspondence courses are herein referred to as subcourses.

duty in some Army hospital but more likely he was on duty as a unit instructor with the National Guard, ORC, or ROTC. Most of the examinations required answers of the essay type and were, therefore, subject to the instructor's interpretation. This resulted in a wide variation in grades for about the same quality of student work.

Following World War II, the department was reopened at the Medical Field Service School, Fort Sam Houston, Tex. Subcourses now are written and administered by the school. We now have a complete centralization of responsibility, uniformity, and far greater efficiency.

Tests and examinations adhere to short-answer requirements, mostly of the true-false or multiple-choice type. A test is given on every lesson and this test and an approved solution is promptly returned to the student, enabling him to recheck his answers. An examination is given on every subcourse and the adjective grade is reported to the student. The present enrollment is shown in table 1. Sixteen and eight-tenths percent of the total Medical Department Reserve officer strength and twenty-four and seven-tenths percent of the National Guard Medical Department officers are enrolled in Medical Department extension courses. Nearly 10,000 subcourse lessons and examinations are being graded each month and the number is increasing by about 500 per month. All papers are corrected and returned to the student, usually within 3 days. This requires a staff of 45 persons.

TABLE 1.—*Enrollment of Army Medical Department personnel in extension courses*

Enlisted men now enrolled	3,150
Officers taking MFSS courses	4,550
Officers taking command and general staff courses	1,300
Total	9,000
Source of enrollees:	
Organized Reserve	6,600
National Guard	1,500
Regular Army	900
Total	9,000

The officers in new Army medical units must initially be mainly of the Medical Service Corps and over 70 percent of the current male officer enrollment in these subcourses is of this Corps. Eleven hundred and thirty female officers are currently enrolled. About 400 new enrollments are approved each month but about 100 are canceled because of the student's inactivity thus making a corrected monthly increase of about 300 students.

Although not all subjects given in the resident course can be taught by correspondence, there are 57 that can be so taught. Since all Army schools are preparing subcourses, each school uses some prepared by other schools, which are called common subcourses. The Medical Field Service School uses 33 such common subcourses. In addition, we transfer our field grade officers enrolled in the extension course to the Command and General Staff College where 20 of their subcourses are made available to them. The original goal was 110 subcourses for Medical Department personnel. Today 55 of these courses are available and are being used by our extension course students. They are kept up to date by frequent revisions. The elements of application, practical examination, and correction must await training assemblies or unit summer training.

Six levels of instruction are prepared for extension courses. The "10" series is primarily for the enlisted men; the "20" series for second lieutenants; the "30" series for first lieutenants; the "40" series for captains; the "50" series for majors; and the "60" series for lieutenant colonels and colonels. The student generally enrolls for an entire series representing several hundred hours of work. The series requested is normally the one prepared for the rank of the applicant. This, however, is not always true. Some specialists have been admitted to the Reserve who have little military education or experience. Such applicants frequently request a lower series than their rank normally receives. If their unit instructor approves, they are enrolled accordingly. The best way for an applicant to enroll is to request the series commensurate with his grade but to state that he desires such review subcourses as may be considered advisable by the administering school. The officer is given what he needs and, largely, what he wants as worked out by direct correspondence.

There are many occasions when an applicant wishes to enroll only for an individual subcourse. For instance, younger officers who have been given an instruction assignment may enroll for the subcourse on "Methods of Instruction" and, in addition, for subcourses that cover the subject that he has had assigned to him to teach. The text and attached memoranda accompanying the lessons constitute the latest principles on the subject matter. While extension courses are designed for personal instruction only, the student who has taken the course can teach the same principles to his unit. Every instructor must make preparations and I know of no first step any more realistic than the one described.

Which subcourses are available at any given time varies because of the state of preparation, revisions, text supply, and student priorities. Because students generally enroll for an entire series that is not important, because the school determines the order in which subcourses

are sent to the student, but when a selected subcourse is requested, the department occasionally must write the student and enclose a mimeographed list of titles showing current availability. Some alternate subcourse is then usually selected by the student. On the other hand, if it develops that he needs the specific subcourse requested as a means of preparing to teach that subject, we find the material he needs in some other department of the school.

Certain National Guard and ORC officers have been provisionally commissioned with inadequate military training and they are generally required to complete the "10" and "20" series within 1 or 2 years. Their subcourses are sent to them 3 at a time so as not to hold them back. In order not to hold any other ambitious student back, the subcourses are sent to a student as fast as he can take them.

Although a complete series of extension courses is not now a prerequisite for promotion in the Reserve, it is one method of fulfilling requirements so that an officer's commanding officer can consider him for promotion. It is desirable for all officers of the Medical Service Corps Reserve to take almost all subcourses from the MFSS and certain administrative subcourses of the Adjutant General's School, especially the one entitled, "Disposition of Records." The Quartermaster School course on "Bookkeeping and Accounting" is also recommended. Eight of the subcourses in other schools are of definite value to company-grade officers. One of these covers hospital construction and is recommended for medical officers who are training for staff and command positions.

Clinical officers should take certain subcourses selected to suit their needs. We do not expect them to take complete series of subcourses. We want to help those who definitely desire help through this medium of training. Professional officers for the most part are earning "points" by other methods. It is a positive challenge to maintain the interest of the medical officers of our Reserve forces in the Reserve program. This is more particularly and understandably so in extension courses. In all fairness these officers desire to remain active but do not have the time to participate.

Medical units are now being organized in a special manner. The present concept of tables of organization for medical units places almost all of the clinical officers in the Professional Complement section. It is considered that the unit will be organized and given extensive training before the professional complement reports to the unit. This means that tremendous basic and unit training responsibility must be assumed by a few officers and the enlisted cadre. Because the training of enlisted cadres is extremely important almost all applicants for extension course enrollment from enlisted men are approved. When these men finish the "10" series, they are permitted to take selected

subcourses in a higher series commensurate with their MOS or their unit or instructional assignments. Many Regular Army enlisted men, through their correspondence activity and proved applicatory capabilities, will be commissioned as second lieutenants in the Medical Service Corps where they will be of great value in a mobilization. In preparing subcourses those subjects dealing with problems to be met in an army in the field have been given preference with second priority being given to the supporting agencies of such a field army.

Some ORC unit commanders wish their personnel to take certain subcourses before their unit's 2-week summer training camp. More units will be required to take such summer training under the new ORC program. Every possible aid is given to such prerequisite extension training as is set up by these unit commanders.

Extension courses may be taken by all military personnel regardless of status. This includes those on the inactive and honorary lists of the Reserve. In view of the close similarity between civil-disaster medical service and medical field service for the Armed Forces, it is expected that the National Security Resources Board, which has charge of planning civil defense on the Federal level will be able to use certain subcourses on evacuating procedures for selected civilian medical and allied science leaders.

Because unification is the order of the day, officers of the Army, Navy, and Air Force may take subcourses in any of the three departments. They should apply for such subcourses through their own branch schools. In January 1950 the Navy had 12 medical subcourses. There are no tests on the lessons, the examination consisting instead of preparing a thesis on the subject matter. One Navy student is taking an Army course and one Army student is taking a Navy course. The Air Force has no extension courses especially prepared for medical personnel but at least 34 Air Force Medical Department Reserve officers are taking Army courses. There may be more because we have had to rely on the student to tell us when he has transferred to the Air Force.

Four new courses are being planned at the Medical Field Service School to parallel our resident instruction on the "Medical Aspects of Atomic Explosion."

Each time our students are circularized with a news letter, warning, or even a Christmas greeting, there is a renewal of activity. This is the reason for the periodic publishing of a news sheet called "Training Report," which is being replaced by the "Medical Department Organized Reserve Corps Training Bulletin." Each branch of the Army will soon publish such a bulletin for their branch. A Reserve officer is assigned full time to the Office of the Surgeon General, De-

partment of the Army, to assist in developing the medical ORC program.

Active duty and retirement credits are given for all subcourses. One credit point is given for 3 hours of work. No officer, however, may be given credit for subcourses in the "10" series. The annual announcement is Department of the Army pamphlet 20–100. Every unit instructor has a copy. It shows the eventual goal for extension courses of all the Army schools. The Medical Field Service School extracts the part that pertains to Medical Department personnel and prints it in a prospectus.

Inquiry from any Medical Department commissioned or enlisted member of the civilian components relative to extension courses may be sent direct to the Medical Field Service School, Fort Sam Houston, Tex.

BOOK REVIEWS AND BOOKS RECEIVED

Publishers submitting books for review are requested to address them as follows:

The Editor,
UNITED STATES ARMED FORCES MEDICAL JOURNAL,
Bureau of Medicine and Surgery, Navy Department,
Washington 25, D. C.

(For review)

TEXTBOOK OF MEDICINE, edited by Sir John Conybeare, K. B. E., M. C., D. M. (Oxon.), F. R. C. P., *Physician to Guy's Hospital, London.* 9th edition. 875 pages, illustrated. The Williams & Wilkins Co., Baltimore, Md., publishers, 1949. Price $8.

This textbook, the first edition of which was published in 1929, covers the entire field of internal medicine. In addition to the usual common medical entities, space is devoted to diseases of infancy, poisonings, aviation medicine, and life-insurance examinations.

The make-up of the book is reminiscent of Cecil's Practice of Medicine and consists of numerous relatively brief articles on individual disease conditions, many signed by the authors. Because of space limitation there is little attempt at discussion and the salient facts are presented in a simple, straight-forward manner. It is noteworthy that the language of the author is such that only rarely is an unfamiliar word or phrase encountered and the reader is not conscious of the book's British origin. Emphases throughout is placed on a clinical approach with little discussion of laboratory findings.

Any medical textbook, no matter how excellent, is soon partially out of date; however, this book emphasizes the rapidity of progress in internal medicine. Although published in 1949, there is meager mention of streptomycin therapy in tuberculosis with its present indications. Aureomycin, chloromycetin, polymyxin, and the newer antibiotics are not included. The entire section on the adrenal glands comprises only three pages, although every practitioner of medicine is now aware of the interest and potential progress that may result from the study of the adrenal steroids.

For the general practitioner, this book will be a valuable reference volume. For the specialist it will be of little use, but it appears to be ideal for the medical student beginning his study of medicine.—*Lt. Col. W. H. Diessner, MC, U. S. A.*

CLINICAL RADIATION THERAPY, by 20 contributors. Edited by Ernest A. Pohle, M. D., Ph D., F. A. C. R., *Professor of Radiology, Chairman, Department of Radiology, University of Wisconsin, Madison, Wis.* 2d edition, enlarged and thoroughly revised. 902 pages; 201 illustrations and a colored plate. Lea & Febiger, Philadelphia, Pa., publishers, 1950. Price $15.

This second edition has been enlarged and thoroughly revised. Radium therapy has been added where practicable, hence the change in title from Clinical Roentgen Therapy to Clinical Radiation Therapy.

The material for this edition has been compiled by Americans from American material. Every effort has been made to have each section written by a well-recognized authority on the subject. There are 14 chapters and 2 supplements. Such important subjects as radiation therapy in "Diseases of the Blood and Blood-Forming Organs," the circulatory system, the respiratory system and breasts, the gastrointestinal tract, the female genital organs, the genito-urinary tract, the nervous system, et cetera, to completely include the entire body and the glands of internal secretion. There is an outstanding and important chapter on "The Civil Liability of the Radiologist." The supplements discuss "Low Intensity Radium Needles" and "Dosage Calculation in Radium Therapy." This is an excellent book, not only for the radiologist, but for everyone in all the fields of medicine.—*Capt. P. Peterson (MC) U. S. N.*

INTRODUCTION TO NEUROPATHOLOGY, by Samuel Pendleton Hicks, M. D., *Departments of Pathology of the Harvard Medical School and the New England Deaconess Hospital; formerly Consultant in Neuropathology, National Naval Medical Center;* and Shields Warren, M. D., *Departments of Pathology of the Harvard Medical School and the New England Deaconess Hospital; Director of the Division of Biology and Medicine, U. S. Atomic Energy Commission.* 494 pages; illustrated. McGraw-Hill Book Company, Inc., New York, N. Y., publishers, 1950. Price $10.

This text achieves the aims of the authors to introduce to medical students and residents in neurology and pathology the fundamentals of disease processes in the nervous system, and to stimulate an interest among general pathologists and neuropsychiatrists toward a closer correlation of their respective viewpoints.

In this work, neuropathology is brought to the general pathologist as an integral part of general pathology, and is presented in such a clear and concise manner that the reader becomes unaware that he is studying a subject which has long been considered complex. The text itself is brief but sufficient, because it is profusely illustrated with excellent, both gross and microscopic, black and white photographs. Charts and schematic drawings are also used to definite advantage. Much of the data presented is based on original work of the senior author. The pathologic physiology of the nervous system is discussed adequately, but the clinical pathologic correlation is neglected. An entire chapter is devoted to congenital anomalies of the nervous system, while only one or two paragraphs are given to such conditions as Wilson's disease and other degenerative diseases of the nervous system which are of special interest to the neuropsychiatrist.

The discussions may be too detailed for the medical student in his study of pathology. The bibliography is good and is quite sufficient. The general pathologist will receive the greatest benefit from this text because it brings neuropathology into the realm of general pathology, treating neurological disorders in their relation to the disease processes in the body as a whole. In spite of a few shortcomings the book is recommended to those interested in neurology and neuropathology.—*Lt. (jg) P. K. Hamilton (MC) U. S. N.*

RESEARCH IN MEDICAL SCIENCE, edited by David E. Green, Ph. D., and W. Eugene Knox, M. D. 492 pages. The Macmillan Co., New York, N. Y., publishers, 1950. Price $6.50.

It is the thesis of the authors that medical research is no longer an arena for clinicians alone. It was their hope to bring a better understanding of fundamental science to clinicians and a better appreciation of medical problems to non-medical investigators. This they have undertaken to accomplish by a series of 26 essays surveying the methods and problems of various specialized fields which impinge on the field of medicine. Although primarily intended for the scientific groups centering around medical interests it is suggested that the intelligent layman will find this a readable book. This reviewer believes the book will prove

profitable and interesting for the scientifically inclined but will make rather heavy going for those who do not have a firm foundation in some field of science. It definitely is not aimed for the layman.

The Anglo-American team of editors has assembled an international list of outstanding authors. The authors have faced the challenge of the editors and have put a strong case for their respective fields. The essays stand independently and each is concluded with its own bibliography. Here Menninger describes psychiatry as a "science" (the quotation marks his) resting on five isolated and inadequately correlated methodological pillars; Burnett discusses viruses; Wolman describes sanitary engineering as an art even though he qualifies it as a hybrid; Montagu describes anthropology as the integrative science of man; and Ingalls approaches the problem of congenital deformities as an epidemic; many other equally stimulating presentations are included.

The book has a table of contents but no index.

Often one hears reference to the romance of the laboratory sciences. Here one feels it astir close at hand. Enthusiasm for the subject runs through these essays like the pulse of a feverish patient. The reader's problem is not to decide which will be interesting but rather which must he read first. This book is recommended for all those who feel they need a lift from the rut of their own specialty and for those who wish to round out their medical scientific background but are pressed for time. This book deserves a wide reading within the medical profession and the allied sciences.—*Commander H. J. Alvis (MC) U. S. N.*

BOOKS RECEIVED

Receipt of the following books is acknowledged. As far as practicable, they will be reviewed at a later date.

SUPERVOLTAGE ROENGENTHERAPY, by Franz Buschke, M. D., Simeon T. Cantril, M. D., and Herbert M. Parker, M. Sc., *from The Tumor Institute of The Swedish Hospital, Seattle, Washington.* 297 pages. Charles C Thomas, Springfield, Ill., publisher. 1950. Price $10.50.

NON-VALVULAR HEART DISEASE, by Henry A. Christian, A. M., M. D., LL. D., Sc. D. (Hon.), M. A. C. P., Hon. F. R. C. P. (Can.), D. S. M. (A. M. A.), *Hersey Professor of the Theory and Practice of Physic, Emeritus, Harvard University; Sometime Clinical Professor of Medicine, Tufts College Medical School; Sometime Physician-in-Chief, Carney Hospital; Sometime Visiting Physician, Beth Israel Hospital; Physician-in-Chief, Emeritus, Peter Bent Brigham Hospital, Boston, Mass.* (Reprinted from Oxford Loose-Leaf Medicine with the same page numbers as that work.) 75 pages. Oxford University Press, New York, N. Y., publishers, 1950. Price $2.

BACTERIAL INFECTION With Special Reference to Dental Practice, by J. L. T. Appleton, B. S., D. D. S., Sc. D., *Professor of Bacteriopathology and Dean, The Thomas W. Evans Museum and Dental Institute School of Dentistry, University of Pennsylvania.* 4th edition, thoroughly revised. 644 pages; illustrated. Lea & Febiger, Philadelphia, Pa., publishers, 1950. Price $10.

A TEXTBOOK OF ORAL HYGIENE AND PREVENTIVE DENISTRY, by Russell W. Bunting, D. D. Sc., *Professor of Dentistry and Dean of the School of Dentistry, University of Michigan,* and collaborators. 240 pages; illustrated. Lea & Febiger, Philadelphia, Pa., publishers, 1950. Price $5.

HANDBOOK OF PHYSICAL MEDICINE AND REHABILITATION, Selections Authorized for Publication by the Council on Physical Medicine and Rehabilitation, American Medical Association. 573 pages; illustrated. Published for the American Medical Association by The Blakiston Company, Philadelphia, Pa., 1950. Price $4.25.

BIOLOGICAL STUDIES WITH POLONIUM, RADIUM, AND POLUTONIUM, edited by Robert M. Fink, Ph. D., *Associate Clinical Professor of Physiological Chemistry, School of Medicine, University of California at Los Angeles; Research Chemist, Birmingham*

Veterans' Administration Hospital, Van Nuys, Calif.; Formerly Assistant Professor of Radiology and Biophysics, School of Medicine and Dentistry, University of Rochester, with 19 contributing authors. 411 pages. McGraw-Hill Book Co., Inc., New York, N. Y., publishers, 1950. Price $3.75.

AMPUTATION PROSTHETIC SERVICE, by Earle H. Daniel, *Director of Prosthetic Service, Institute of Physical Medicine and Rehabilitation, New York University, Bellevue Medical Center. Prosthetic Consultant to: Bellevue, City, Goldwater Memorial, Metropolitan, and University Hospitals, New York, N. Y.,* with foreword by Howard A. Rusk, M. D., *Professor and Chairman of the Department of Physical Medicine and Rehabilitation, New York University College of Medicine; Director, Institute of Physical Medicine and Rehabilitation, New York University, Bellevue Medical Center.* 327 pages; illustrated. The Williams & Wilkins Co., Baltimore, Md., publishers, 1950. Price $7.

THE ABNORMAL PNEUMOENCEPHALOGRAM, by Leo M. Davidoff, M. D., *Director of Neurological Surgery, Beth Israel Hospital, New York City; Clinical Professor of Neurosurgery, New York University, Postgraduate Medical School,* and Bernard S. Epstein, M. D., *Associate Radiologist, The Jewish Hospital of Brooklyn, Brooklyn, N. Y., and Instructor in Clinical Radiology, Long Island College of Medicine.* 506 pages, illustrated. Lea & Febiger, Philadelphia, Pa., publishers, 1950. Price $15.

MEDICAL PHYSICS, Volume II. Editor-in-Chief Otto Glasser, Ph. D., F. A. C. R., *Diplomate in Radiological Physics, American Board of Radiology; Professor of Biophysics, Frank E. Bunts Educational Institute; Head, Department of Biophysics, Cleveland Clinic Foundation; Consultant, U. S. Veterans' Administration, Washington, D. C.,* and editorial assistant Jessie C. Tucker, *Cleveland, Ohio,* and associate editors. 1,227 pages; 978 illustrations. The Year Book Publishers, Inc., Chicago, Ill., publishers, 1950. Price $25.

CORONARY CIRCULATION IN HEALTH AND DISEASE, by Donald E. Gregg, M. S., Ph. D., M. D., *Chief Research Physician, Medical Department, Field Research Laboratory, Fort Knox, Ky.* 227 pages; illustrated. Lea & Febiger, Philadelphia, Pa., publishers, 1950. Price $4.50.

WOMAN'S SURGEON, The Life Story of J. Marion Sims, by Seale Harris, M. D., with the collaboration of Frances Williams Browin. 432 pages; illustrated. The Macmillan Co., New York, N. Y., publishers, 1950. Price $5.

THE PHYSIOLOGY OF TISSUES AND ORGANS, An Introduction to the Study of Systematic Physiology, by Douglas H. K. Lee, M. D., M. Sc., D. T. M., F. R. A. C. P., *Professor of Physiological Climatology, The Johns Hopkins University, Baltimore, Md.; formerly Professor of Physiology, University of Queensland, Australia.* 159 pages; illustrated. Charles C Thomas, Springfield, Ill., publisher, 1950. Price $4.

ACRYLIC INLAYS, CROWNS, AND BRIDGES, by Irwin Robert Levy, D. D. S., *formerly Director, American Training Institute; Chief of Dental Clinic, Big Sisters Organization; Assistant Dentist, Mt. Sinai Hospital, New York City; Director, Dental Division, Eastern School for Physician's Aides; Author of "Textbook for Dental Assistants."* 128 pages; illustrated. Lea & Febiger, Philadelphia, Pa., publishers, 1950. Price $3.75.

PROCTOLOGY IN GENERAL PRACTICE, by J. Peerman Nesselrod, B. S., M. S., M. Sc. (Med.), F. A. C. S., F. A. P. S., *Associate in Surgery, Northwestern University Medical School; Associate Surgeon, Division of Proctology, Evanston Hospital, Evanston, Ill.; Certified by the Central Certifying Committee in Proctology (Founders' Group) of the American Board of Surgery; Commander (MC), U. S. N. R.* 276 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950. Price $6.00.

PENICILLIN AND STREPTOMYCIN IN THE TREATMENT OF INFECTIONS, by Chester S. Keefer, M. S., M. D., Sc. D. (Hon.), *Wade Professor of Medicine, Boston University School of Medicine; Director of Evans Memorial and Physician-in-Chief, Massachusetts Memorial Hospital, Boston; Chairman, Committee on Chemotherapeutic and Other Agents, National Research Council; Consultant to the Committee on Medical Research, Office of Scientific Research and Development, Washington, D. C.,* and Donald G. Anderson, M. D., *Instructor in Medicine, Boston University School of Medicine; Research Fellow in Medicine at Evans Memorial; Assistant Visiting Physician, Massachusetts Memorial Hospital, Boston, Mass.,* edited by Henry A. Christian, A. M., M. D., LL. D., Sc. D. (Hon.), M. A. C. P., Hon. F. R. C. P. (Can.), D. S. M. (A. M. A.), *Hersey Professor of the Theory and Practice of Physic, Emeritus, Harvard University; Sometime Clinical Professor of Medicine, Tufts Medical*

School; Sometime Physician-in-Chief, Carney Hospital; Sometime Visiting Physician, Beth Israel Hospital; Physician-in-Chief, Emeritus, Peter Bent Brigham Hospital, Boston, Mass. (Reprinted from Oxford Loose-Leaf Medicine with the same page numbers as in that work). 111 pages. Oxford University Press, New York, N. Y., publishers, 1950. Price $2.50.

GUIDING LEARNING EXPERIENCE, Principles of Progressive Education Applied to Nursing Education, by Maude B. Muse, R. N., A. M., *formerly, Associate Professor of Nursing Education, Teachers College, Columbia University.* 617 pages. The Macmillan Co., New York, N. Y., publishers, 1950. Price $4.50.

YOU AND YOUR HEART, A Clinic for Laymen on the Heart and Circulation, by H. M. Marvin, M. D., T. Duckett Jones, M. D., Irvine H. Page, M. D., Irving S. Wright, M. D., and David D. Rutstein, M. D., with foreword by Paul D. White, M. D. 306 pages; illustrated. Random House, New York, N. Y., publishers, 1950. Price $3.

THE PRACTICE OF MEDICINE, by Jonathan Campbell Meakins, C. B. E., M. D., LL. D., D. Sc., *formerly Professor of Medicine and Director of the Department of Medicine, McGill University; formerly Physician-in-Chief, Royal Victoria Hospital, Montreal; formerly Professor of Therapeutics and Clinical Medicine, University of Edinburgh; Fellow of the Royal Society of Edinburgh; Fellow of the Royal Society of Canada; Fellow of the Royal College of Physicians, London; Fellow of the Royal College of Physicians, Edinburgh; Honorary Fellow of the Royal College of Surgeons, Edinburgh; Fellow of the Royal College of Physicians, Canada; Fellow of the American College of Physicians; Honorary Fellow of the Royal Society of Medicine.* 5th edition. 1,558 pages; illustrated. The C. V. Mosby Co., St. Louis, Mo., publishers, 1950. Price $13.50.

1949 YEAR BOOK OF ENDOCRINOLOGY, METABOLISM AND NUTRITION (December 1948–January 1949). Endocrinology edited by Willard O. Thompson, M. D., *Clinical Professor of Medicine, University of Illinois College of Medicine; Attending Physician (Senior Staff, Henrotin Hospital; Attending Physician, Grant Hospital of Chicago.* Metabolism and Nutrition edited by Tom D. Spies, M. D., *Chairman, Department of Nutrition and Metabolism, Northwestern University School of Medicine; Director, Nutrition Clinic, Hillman Hospital, Birmingham, Ala.* 545 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., publishers, 1950. Price $4.75.

CLINICAL ORTHOPTIC PROCEDURE, A Reference Book on Clinical Methods of Orthoptics, by William Smith, O. D., *Associate Instructor in Optometry and Instructor of Orthoptics and Visual Training, Massachusetts School of Optometry, Boston, Mass.* 393 pages; illustrated. The C. V. Mosby Co., St. Louis, Mo., publishers, 1950. Price $8.

THE ETHICAL BASIS OF MEDICAL PRACTICE, by Willard L. Sperry, *Dean of the Harvard Divinity School,* with a foreword by J. Howard Means, M. D. 185 pages. Paul B. Hoeber, Inc., New York, N. Y., publishers, 1950. Price $2.50.

THE MANAGEMENT OF THE PATIENT WITH SEVERE BRONCHIAL ASTHMA, by Maurice S. Segal, M. D., *Assistant Professor in Medicine, Tufts College Medical School; Director, Department of Inhalational Therapy, Boston City Hospital, Boston, Mass.* (Publication Number 76, American Lecture Series.) 158 pages. Charles C Thomas, Springfield, Ill., publisher, 1950. Price $3.50.

THE CAUSATION AND TREATMENT OF DELAYED UNION IN FRACTURES OF THE LONG BONE, by Kenneth W. Starr, O. B. E., E. D., M. B., B. S. (Syd.), M. S. (Melb.), F. R. C. S. (Eng.), F. A. C. S., F. R. A. C. S., *Surgeon, Sydney Hospital, New South Wales; Visiting Surgeon, Concord Military Hospital; Consulting Plastic Surgeon, Faculty of Dentistry, University of Sydney; Member of the Court of Examiners, Royal Australasian College of Surgeons; Lt.-Col. (R. of O.), A. A. M. C., late Officer Commanding Surgical Division.* 233 pages; illustrated. The C. V. Mosby Co., St. Louis, Mo., publishers, 1947. Price $9.

LIPIDOSES, Diseases of the Cellular Lipid Metabolism, by Siegfried J. Thannhauser, M. D., Ph. D., *Associate Professor of Medicine, Tufts College Medical School; Associate Physician-in-Chief, Joseph H. Pratt Diagnostic Hospital, Boston, Mass.,* edited by Henry A. Christian, A. M., M. D., LL. D., Sc. D. (Hon.), M. A. C. P., Hon. F. R. C. P. (Can.), D. S. M. (A. M. A.), *Hersey Professor of the Theory and Practice of Physic, Emeritus, Harvard University; Sometime Clinical Professor of Medicine, Tufts Medical School; Sometime Physician-in-Chief, Carney Hospital; Sometime Visiting Physician, Beth Israel Hospital; Physician-in-Chief, Emeritus, Peter Bent Brigham Hospital, Boston, Mass.* (Reprinted from Oxford Loose-Leaf Medicine with the same page numbers as in that work). 605 pages; illustrated. Oxford University Press, New York, N. Y., publishers, 1950. Price $12.

A GUIDE TO GENERAL MEDICAL PRACTICE, by Martin G. Vorhaus, M. D., *Attending Physician, Hospital for Joint Diseases, New York City.* 244 pages. The Macmillan Co., New York, N. Y., publishers, 1950. Price $3.50.

TEXTBOOK OF ENDOCRINOLOGY, edited by Robert H. Williams, M. D., *Executive Officer and Professor of Medicine, University of Washington Medical School, Seattle,* with the collaboration of Peter H. Forsham, Harry B. Friedgood, John Eager Howard, Edwin J. Kepler, William Locke, L. Harry Newburgh, Edward C. Reifenstein, Jr., William W. Scott, George Van S. Smith, George W. Thorn, and Lawson Wilkins. 793 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950.

A PRIMER FOR DIABETIC PATIENTS, by Russell M. Wilder, M. D., Ph. D., F. A. C. P., *Professor and Chief of the Department of Medicine of the Mayo Foundation, University of Minnesota; Senior Consultant in the Division of Medicine, Mayo Clinic.* 9th edition. 200 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950. Price $2.25.

NURSING CARE OF THE SURGICAL PATIENT (formerly Textbook of Surgical Nursing, 4th edition, by McFee and Keller), by John Pettit West, M. D., *Attending Surgeon, St. Luke's Hospital, New York; Assistant Attending Surgeon, New York Hospital, New York; Assistant Professor of Clinical Surgery, Cornell University Medical College, New York;* Manelva Wylie Keller, B. S., R. N., *Formerly, Chief Operating Room Nurse, St. Luke's Hospital, New York, and Anesthetist, St Luke's Hospital, New York;* and Elizabeth Harmon, B. A., R. N., *Instructor in Surgical Nursing, Cornell University-New York Hospital School of Nursing, New York; Assistant Head, Surgical Nursing Service, New York Hospital, New York.* 5th edition. 500 pages; illustrated. The Macmillan Co., New York, N. Y., publishers, 1950. Price $4.